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PASSWORD:

TERMINAL (ENTER 1, 2, 3, OR ?):2

\* \* \* \* \* Welcome to STN International \* \* \* \* \*

NEWS	1		Web Page URLs for STN Seminar Schedule - N. America
NEWS	2		"Ask CAS" for self-help around the clock
NEWS	3	SEP 01	New pricing for the Save Answers for SciFinder Wizard within STN Express with Discover!
NEWS	4	OCT 28	KOREAPAT now available on STN
NEWS	5	NOV 30	PHAR reloaded with additional data
NEWS	6	DEC 01	LISA now available on STN
NEWS	7	DEC 09	12 databases to be removed from STN on December 31, 2004
NEWS	8	DEC 15	MEDLINE update schedule for December 2004
NEWS	9	DEC 17	ELCOM reloaded; updating to resume; current-awareness alerts (SDIs) affected
NEWS	10	DEC 17	COMPUAB reloaded; updating to resume; current-awareness alerts (SDIs) affected
NEWS	11	DEC 17	SOLIDSTATE reloaded; updating to resume; current-awareness alerts (SDIs) affected
NEWS	12	DEC 17	CERAB reloaded; updating to resume; current-awareness alerts (SDIs) affected
NEWS	13	DEC 17	THREE NEW FIELDS ADDED TO IFIPAT/IFIUDB/IFICDB
NEWS	14	DEC 30	EPFULL: New patent full text database to be available on STN
NEWS	15	DEC 30	CAPLUS - PATENT COVERAGE EXPANDED
NEWS	16	JAN 03	No connect-hour charges in EPFULL during January and February 2005
NEWS	17	FEB 25	CA/CAPLUS - Russian Agency for Patents and Trademarks (ROSPATENT) added to list of core patent offices covered
NEWS	18	FEB 10	STN Patent Forums to be held in March 2005
NEWS	19	FEB 16	STN User Update to be held in conjunction with the 229th ACS National Meeting on March 13, 2005
NEWS	20	FEB 28	PATDPAFULL - New display fields provide for legal status data from INPADOC
NEWS	21	FEB 28	BABS - Current-awareness alerts (SDIs) available
NEWS	22	FEB 28	MEDLINE/LMEDLINE reloaded
NEWS	23	MAR 02	GBFULL: New full-text patent database on STN
NEWS	24	MAR 03	REGISTRY/ZREGISTRY - Sequence annotations enhanced
NEWS EXPRESS			JANUARY 10 CURRENT WINDOWS VERSION IS V7.01a, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 10 JANUARY 2005
NEWS HOURS			STN Operating Hours Plus Help Desk Availability
NEWS INTER			General Internet Information
NEWS LOGIN			Welcome Banner and News Items
NEWS PHONE			Direct Dial and Telecommunication Network Access to STN
NEWS WWW			CAS World Wide Web Site (general information)

Enter NEWS followed by the item number or name to see news on that specific topic.

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\* \* \* \* \* STN Columbus \* \* \* \* \*

FILE 'HOME' ENTERED AT 15:17:55 ON 03 MAR 2005

=> fil reg

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

0.21

0.21

FILE 'REGISTRY' ENTERED AT 15:18:07 ON 03 MAR 2005

USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.

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Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 2 MAR 2005 HIGHEST RN 841200-41-7

DICTIONARY FILE UPDATES: 2 MAR 2005 HIGHEST RN 841200-41-7

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 18, 2005

Please note that search-term pricing does apply when conducting SmartSELECT searches.

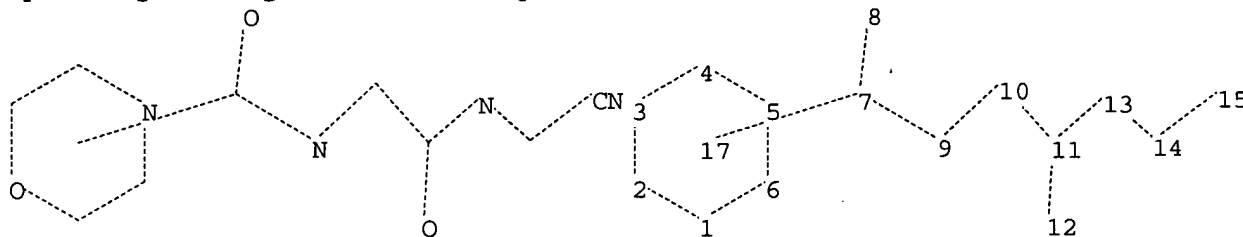
Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at:

<http://www.cas.org/ONLINE/DBSS/registryss.html>

=>

Uploading C:\Program Files\Stnexp\Queries\10758893.str



chain nodes :

7 8 9 10 11 12 13 14 15

ring nodes :

1 2 3 4 5 6

chain bonds :

7-8 7-9 9-10 10-11 11-12 11-13 13-14 14-15

ring bonds :

1-2 1-6 2-3 3-4 4-5 5-6

exact/norm bonds :

1-2 1-6 2-3 3-4 4-5 5-6 7-8 7-9 9-10 10-11 11-12 11-13 13-14 14-15

isolated ring systems :

containing 1 :

Match level :

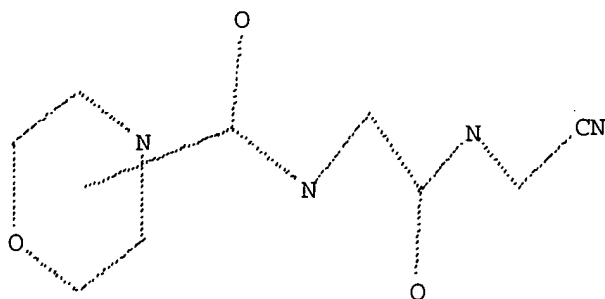
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:CLASS 8:CLASS 9:CLASS 10:CLASS  
11:CLASS 12:CLASS 13:CLASS 14:CLASS 15:CLASS 17:CLASS

L1 STRUCTURE UPLOADED

=> d

L1 HAS NO ANSWERS

L1 STR



Structure attributes must be viewed using STN Express query preparation.

=> s l1

SAMPLE SEARCH INITIATED 15:18:30 FILE 'REGISTRY'

SAMPLE SCREEN SEARCH COMPLETED - 28 TO ITERATE

100.0% PROCESSED 28 ITERATIONS

5 ANSWERS

SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE \*\*COMPLETE\*\*

BATCH \*\*COMPLETE\*\*

PROJECTED ITERATIONS: 243 TO 877

PROJECTED ANSWERS: 5 TO 234

L2 5 SEA SSS SAM L1

=> s l1 full

FULL SEARCH INITIATED 15:18:33 FILE 'REGISTRY'

FULL SCREEN SEARCH COMPLETED - 478 TO ITERATE

100.0% PROCESSED 478 ITERATIONS

79 ANSWERS

SEARCH TIME: 00.00.01

L3 79 SEA SSS FUL L1

=> s l3 and caplus/lc

44463264 CAPLUS/LC

L4 79 L3 AND CAPLUS/LC

=> fil caplus

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

165.93

166.14

FILE 'CAPLUS' ENTERED AT 15:18:42 ON 03 MAR 2005

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FILE COVERS 1907 - 3 Mar 2005 VOL 142 ISS 10  
FILE LAST UPDATED: 2 Mar 2005 (20050302/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s l4

L5 9 L4

=> d ibib abs hitstr 1-9

L5 ANSWER 1 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:267319 CAPLUS

DOCUMENT NUMBER: 140:304079

TITLE: Preparation of iodotyrosine cyanomethylamides as  
Cathepsin B inhibitors

INVENTOR(S): Burrill, Leland C., II; Palmer, James T.; Rydzewski,  
Robert M.

PATENT ASSIGNEE(S): Axys Pharmaceuticals, Inc., USA

SOURCE: PCT Int. Appl., 42 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

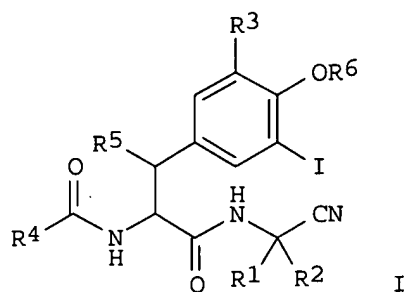
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004026851	A1	20040401	WO 2003-US29545	20030916
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			

PRIORITY APPLN. INFO.: US 2002-412368P P 20020920

OTHER SOURCE(S): MARPAT 140:304079

GI



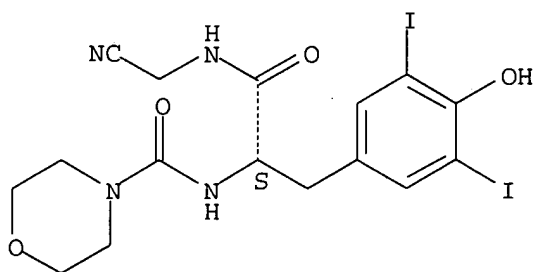
AB Title compds. [I; R1, R2 = H, alkyl, haloalkyl, hydroxyalkyl, aryl, aralkyl; R1R2 = atoms to form a cycloalkyl, heterocycloalkyl ring; R3 = alkyl, iodo; R4 = (substituted) aryl, heteroaryl, heterocycloalkyl; R5, R6 = H, alkyl], were prepared as Cathepsin B inhibitors (no data). Thus, 4-morpholinobenzoic acid hydrochloride, hydroxybenzotriazole, Et3N, and EDC were stirred 30 min in DMF; L-3,5-diiiodotyrosine, Et3N, and H2O in DMF were added followed by stirring for 16 h to give (S)-3-(4-hydroxy-3,5-diiiodophenyl)-2-(4-morpholin-4-ylbenzoylamino)propionic acid. The latter was stirred overnight with aminoacetonitrile hydrochloride, HBTU, and N-methylmorpholine in DMF to give (S)-N-[1-(cyanomethylcarbamoyl)-2-(4-hydroxy-3,5-diiiodophenyl)ethyl]-4-morpholin-4-ylbenzamide.

IT **676477-50-2P**  
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (preparation of iodotyrosine cyanomethylamides as Cathepsin B inhibitors)

RN 676477-50-2 CAPLUS

CN 4-Morpholinecarboxamide, N-[(1S)-2-[(cyanomethyl)amino]-1-[(4-hydroxy-3,5-diiiodophenyl)methyl]-2-oxoethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 2 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2003:55370 CAPLUS

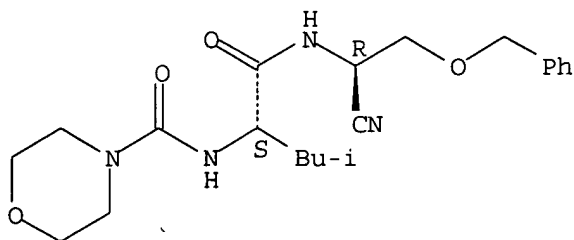
DOCUMENT NUMBER: 140:5280

TITLE: Design and synthesis of dipeptide nitriles as reversible and potent Cathepsin S inhibitors. [Erratum to document cited in CA138:56234]

AUTHOR(S): Ward, Yancey D.; Thomson, David S.; Frye, Leah L.; Cywin, Charles L.; Morwick, Tina; Emmanuel, Michel J.; Zindell, Renee; McNeil, Daniel; Bekkali, Younes; Girardot, Marc; Hrapchak, Matt; DeTuri, Molly; Crane, Kathy; White, Della; Páv, Susan; Wang, Yong; Hao, Ming-Hong; Grygon, Christine A.; Labadia, Mark E.; Freeman, Dorothy M.; Davidson, Walter; Hopkins, Jerry

L.; Brown, Maryanne L.; Spero, Denice M.  
 CORPORATE SOURCE: Boehringer Ingelheim Pharmaceuticals, Ridgefield, CT,  
 06877-0368, USA  
 SOURCE: Journal of Medicinal Chemistry (2003), 46(5), 882  
 CODEN: JMCMAR; ISSN: 0022-2623  
 PUBLISHER: American Chemical Society  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB The name of author Marc Girardot was incorrect in the version published on  
 the Web 10/31/2002 (ASAP) and in the Dec. 5, 2002 issue (Volume 45, Number 25,  
 pp 5471-5482). The correct electronic version of the manuscript was  
 published on 01/20/2003.  
 IT **479091-78-6**  
 RL: PRP (Properties)  
 (crystal structure of cathepsin S cocrystd. with dipeptide nitrile as  
 its reversible inhibitor (Erratum))  
 RN 479091-78-6 CAPLUS  
 CN 4-Morpholinecarboxamide, N-[(1S)-1-[[[(1R)-1-cyano-2-  
 (phenylmethoxy)ethyl]amino]carbonyl]-3-methylbutyl]-, compd. with  
 cathepsin S (1:1) (9CI) (CA INDEX NAME)  
 CM 1  
 CRN 290816-77-2  
 CMF C21 H30 N4 O4

Absolute stereochemistry.

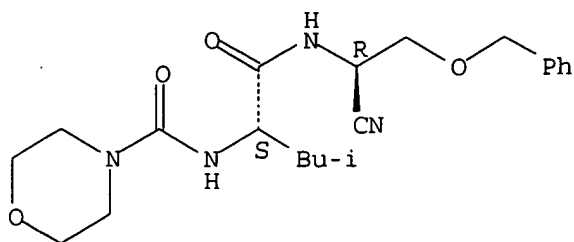


CM 2  
 CRN 71965-46-3  
 CMF Unspecified  
 CCI MAN

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

IT **290816-77-2P**  
 RL: BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic  
 preparation); BIOL (Biological study); PREP (Preparation)  
 (preparation and biol. activity of dipeptide nitriles as reversible and  
 potent cathepsin S inhibitors (Erratum))  
 RN 290816-77-2 CAPLUS  
 CN 4-Morpholinecarboxamide, N-[(1S)-1-[[[(1R)-1-cyano-2-  
 (phenylmethoxy)ethyl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX  
 NAME)

Absolute stereochemistry.



IT 225119-70-0P 290816-49-8P 290816-76-1P  
 290816-78-3P 290816-82-9P 290816-83-0P  
 290816-89-6P 290816-91-0P 290817-01-5P  
 290817-02-6P 290817-03-7P 290817-12-8P  
 479091-50-4P 479091-51-5P 479091-52-6P  
 479091-53-7P 479091-54-8P 479091-55-9P  
 479091-56-0P 479091-57-1P 479091-58-2P  
 479091-59-3P 479091-60-6P 479091-61-7P  
 479091-62-8P 479091-63-9P 479091-64-0P  
 479091-65-1P 479091-66-2P 479091-67-3P  
 479091-68-4P 479091-69-5P

RL: BSU (Biological study, unclassified); SPN (Synthetic preparation);

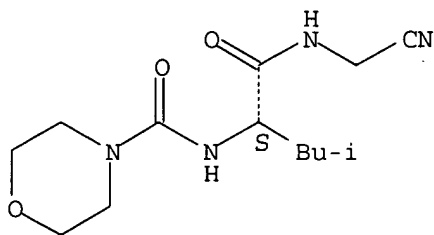
BIOL (Biological study); PREP (Preparation)

(preparation and biol. activity of dipeptide nitriles as reversible and  
 potent cathepsin S inhibitors (Erratum))

RN 225119-70-0 CAPLUS

CN 4-Morpholinecarboxamide, N-[(1S)-1-[[[(cyanomethyl)amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

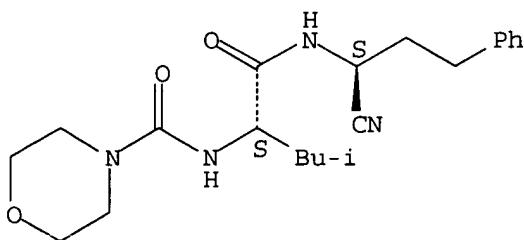
Absolute stereochemistry.



RN 290816-49-8 CAPLUS

CN 4-Morpholinecarboxamide, N-[(1S)-1-[[[(1S)-1-cyano-3-phenylpropyl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

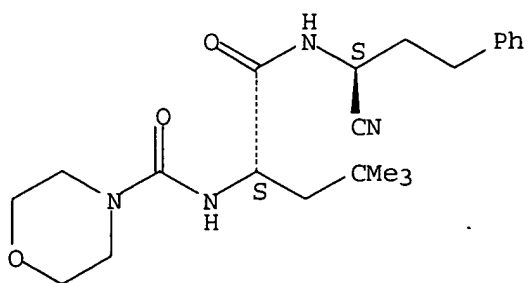
Absolute stereochemistry.



RN 290816-76-1 CAPLUS

CN 4-Morpholinecarboxamide, N-[(1S)-1-[[[(1S)-1-cyano-3-phenylpropyl]amino]carbonyl]-3,3-dimethylbutyl]- (9CI) (CA INDEX NAME)

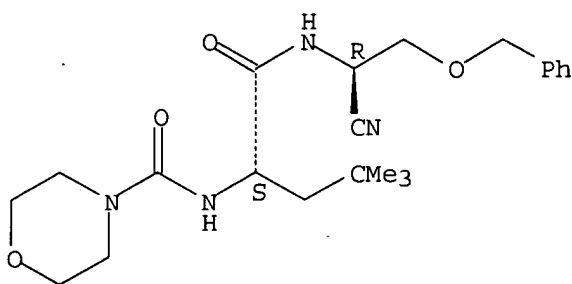
Absolute stereochemistry.



RN 290816-78-3 CAPLUS

CN 4-Morpholinecarboxamide, N-[(1S)-1-[[[(1R)-1-cyano-2-(phenylmethoxy)ethyl]amino]carbonyl]-3,3-dimethylbutyl]- (9CI) (CA INDEX NAME)

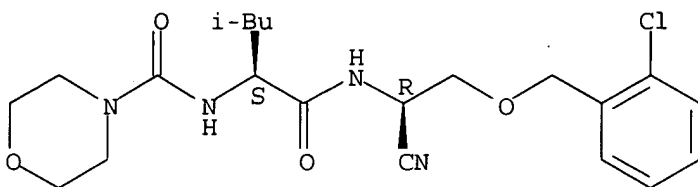
Absolute stereochemistry.



RN 290816-82-9 CAPLUS

CN 4-Morpholinecarboxamide, N-[(1S)-1-[[[(1R)-2-[(2-chlorophenyl)methoxy]-1-cyanoethyl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

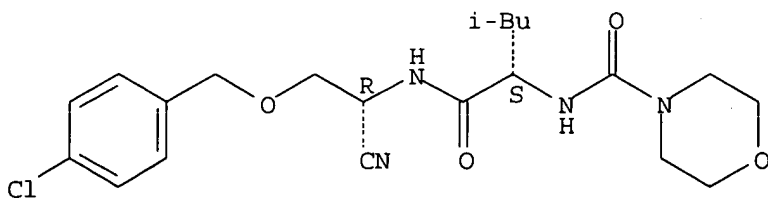
Absolute stereochemistry.



RN 290816-83-0 CAPLUS

CN 4-Morpholinecarboxamide, N-[(1S)-1-[[[(1R)-2-[(4-chlorophenyl)methoxy]-1-cyanoethyl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

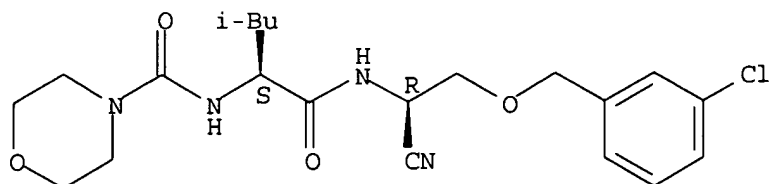


RN 290816-89-6 CAPLUS

CN 4-Morpholinecarboxamide, N-[(1S)-1-[[[(1R)-2-[(3-chlorophenyl)methoxy]-1-cyanoethyl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)



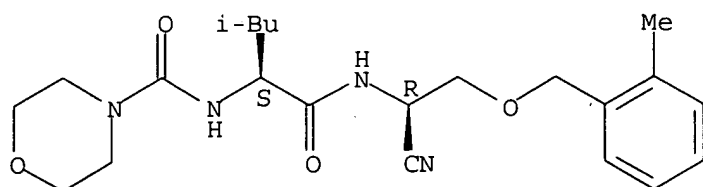
Absolute stereochemistry.



RN 290816-91-0 CAPLUS

CN 4-Morpholinecarboxamide, N-[(1S)-1-[[[(1R)-1-cyano-2-[(2-methylphenyl)methoxy]ethyl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

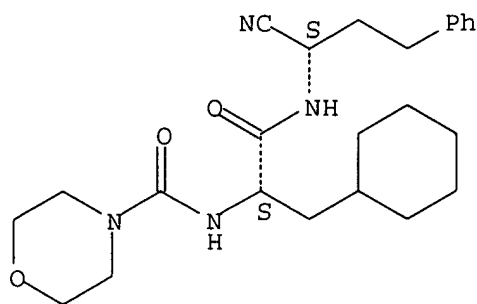
Absolute stereochemistry.



RN 290817-01-5 CAPLUS

CN 4-Morpholinecarboxamide, N-[(1S)-2-[[[(1S)-1-cyano-3-phenylpropyl]amino]-1-(cyclohexylmethyl)-2-oxoethyl]- (9CI) (CA INDEX NAME)

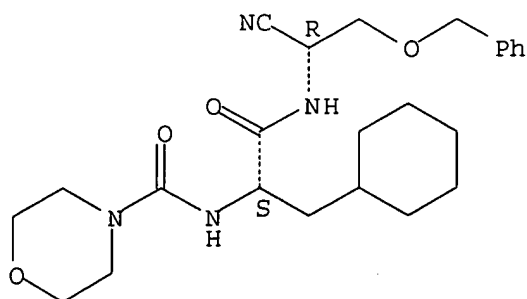
Absolute stereochemistry.



RN 290817-02-6 CAPLUS

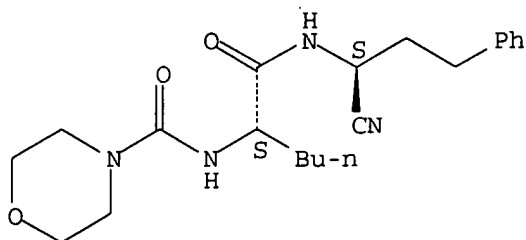
CN 4-Morpholinecarboxamide, N-[(1S)-2-[[[(1R)-1-cyano-2-(phenylmethoxy)ethyl]amino]-1-(cyclohexylmethyl)-2-oxoethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



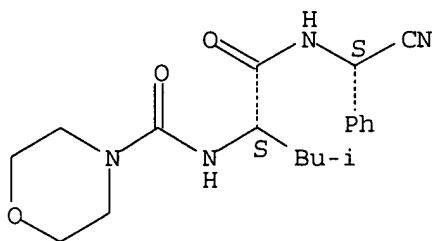
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CN 4-Morpholinecarboxamide, N-[(1S)-1-[[[(1S)-1-cyano-3-phenylpropyl]amino]carbonyl]pentyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



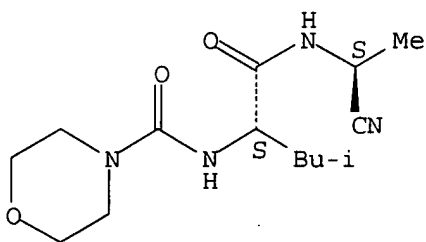
RN 290817-12-8 CAPLUS  
CN 4-Morpholinecarboxamide, N-[(1S)-1-[[[(S)-cyanophenylmethyl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



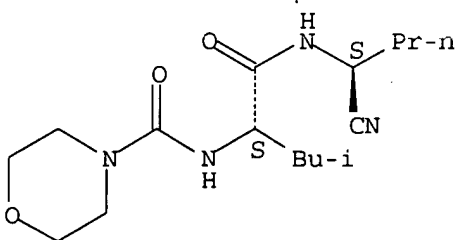
RN 479091-50-4 CAPLUS  
CN 4-Morpholinecarboxamide, N-[(1S)-1-[[[(1S)-1-cyanoethyl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 479091-51-5 CAPLUS  
CN 4-Morpholinecarboxamide, N-[(1S)-1-[[[(1S)-1-cyanobutyl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

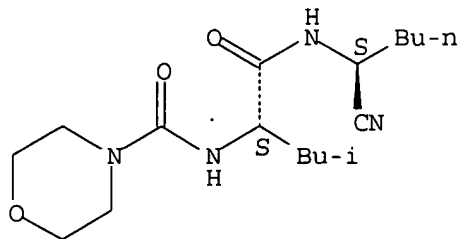
Absolute stereochemistry.



RN 479091-52-6 CAPLUS

CN 4-Morpholinecarboxamide, N-[(1S)-1-[[[(1S)-1-cyanopentyl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

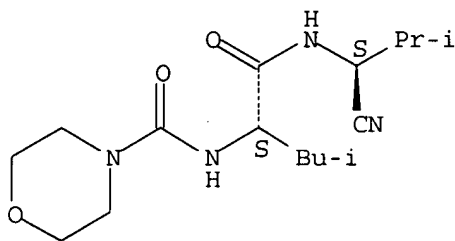
Absolute stereochemistry.



RN 479091-53-7 CAPLUS

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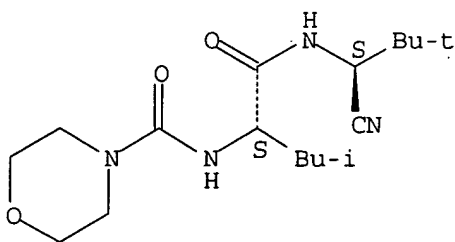
Absolute stereochemistry.



RN 479091-54-8 CAPLUS

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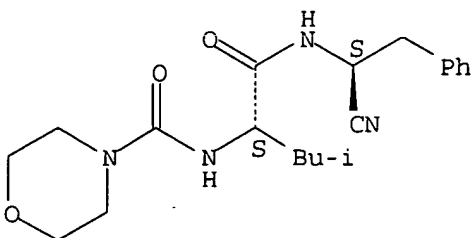
Absolute stereochemistry.



RN 479091-55-9 CAPLUS

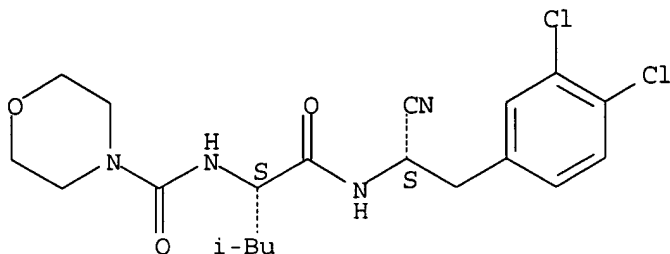
CN 4-Morpholinecarboxamide, N-[(1S)-1-[[[(1S)-1-cyano-2-phenylethyl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



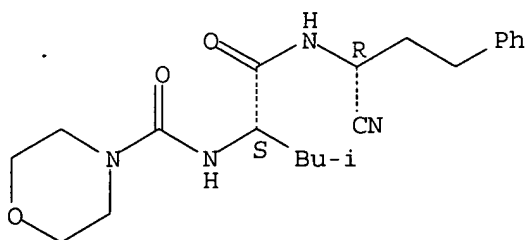
RN 479091-56-0 CAPLUS  
 CN 4-Morpholinecarboxamide, N-[(1S)-1-[[[(1S)-1-cyano-2-(3,4-dichlorophenyl)ethyl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



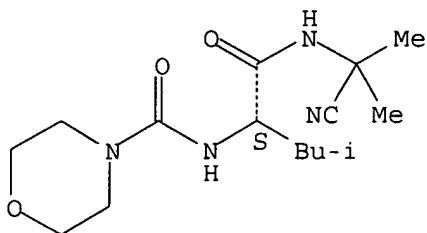
RN 479091-57-1 CAPLUS  
 CN 4-Morpholinecarboxamide, N-[(1S)-1-[[[(1R)-1-cyano-3-phenylpropyl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



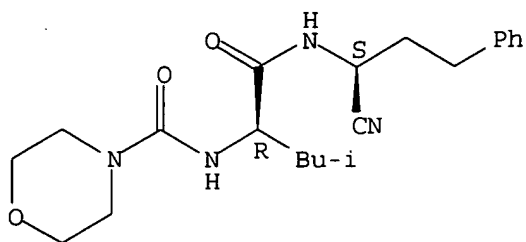
RN 479091-58-2 CAPLUS  
 CN 4-Morpholinecarboxamide, N-[(1S)-1-[[[1-cyano-1-methylethyl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 479091-59-3 CAPLUS  
 CN 4-Morpholinecarboxamide, N-[(1R)-1-[[[(1S)-1-cyano-3-phenylpropyl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

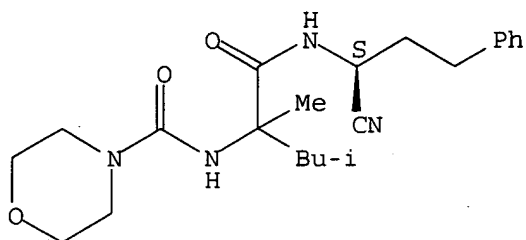
Absolute stereochemistry.



RN 479091-60-6 CAPLUS

CN 4-Morpholinecarboxamide, N-[1-[[[(1S)-1-cyano-3-phenylpropyl]amino]carbonyl]-1,3-dimethylbutyl]- (9CI) (CA INDEX NAME)

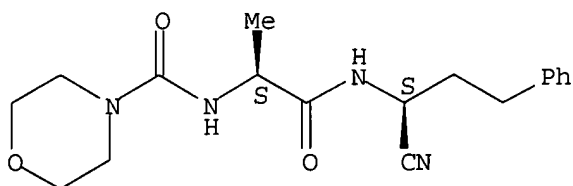
Absolute stereochemistry.



RN 479091-61-7 CAPLUS

CN 4-Morpholinecarboxamide, N-[(1S)-2-[[[(1S)-1-cyano-3-phenylpropyl]amino]-1-methyl-2-oxoethyl]- (9CI) (CA INDEX NAME)

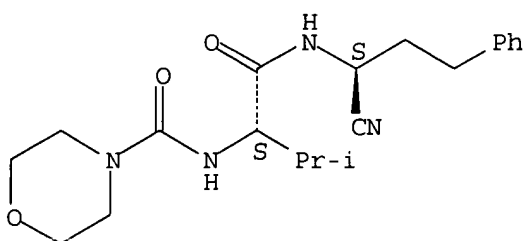
Absolute stereochemistry.



RN 479091-62-8 CAPLUS

CN 4-Morpholinecarboxamide, N-[(1S)-1-[[[(1S)-1-cyano-3-phenylpropyl]amino]carbonyl]-2-methylpropyl]- (9CI) (CA INDEX NAME)

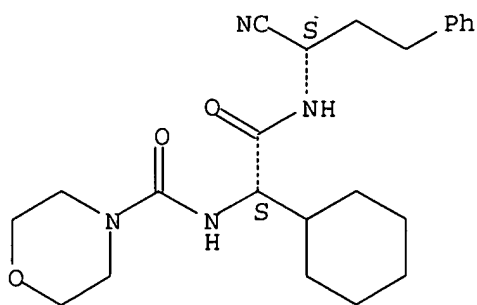
Absolute stereochemistry.



RN 479091-63-9 CAPLUS

CN 4-Morpholinecarboxamide, N-[(1S)-2-[[[(1S)-1-cyano-3-phenylpropyl]amino]-1-cyclohexyl-2-oxoethyl]- (9CI) (CA INDEX NAME)

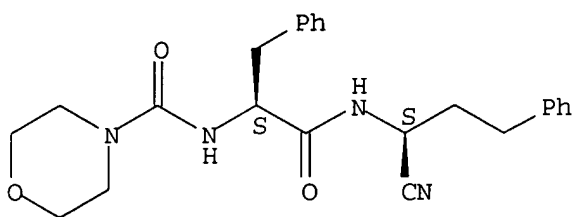
Absolute stereochemistry.



RN 479091-64-0 CAPLUS

CN 4-Morpholinecarboxamide, N-[(1S)-2-[[[(1S)-1-cyano-3-phenylpropyl]amino]-2-oxo-1-(phenylmethyl)ethyl]- (9CI) (CA INDEX NAME)

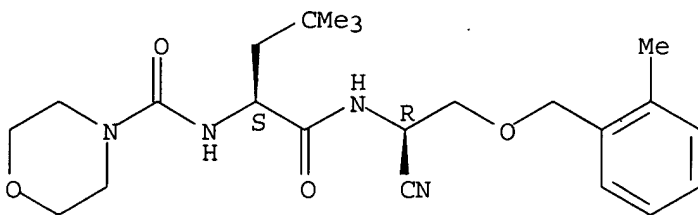
Absolute stereochemistry.



RN 479091-65-1 CAPLUS

CN 4-Morpholinecarboxamide, N-[(1S)-1-[[[(1R)-1-cyano-2-[(2-methylphenyl)methoxy]ethyl]amino]carbonyl]-3,3-dimethylbutyl]- (9CI) (CA INDEX NAME)

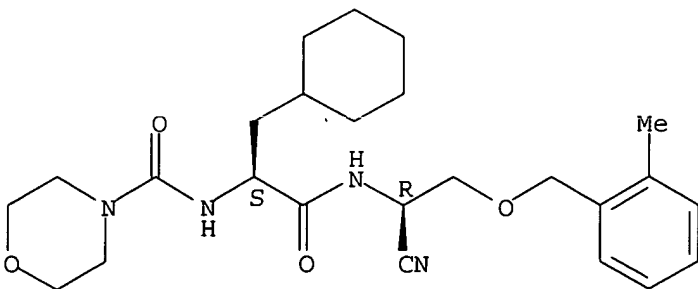
Absolute stereochemistry.



RN 479091-66-2 CAPLUS

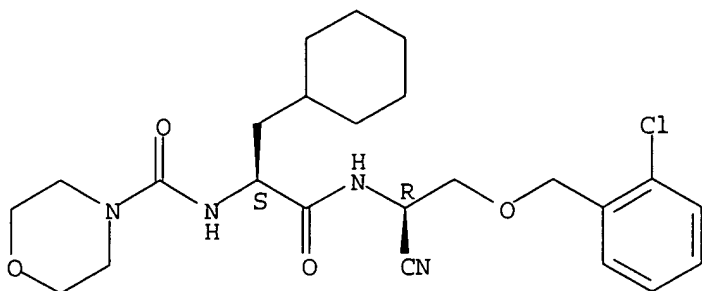
CN 4-Morpholinecarboxamide, N-[(1S)-2-[[[(1R)-1-cyano-2-[(2-methylphenyl)methoxy]ethyl]amino]-1-(cyclohexylmethyl)-2-oxoethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



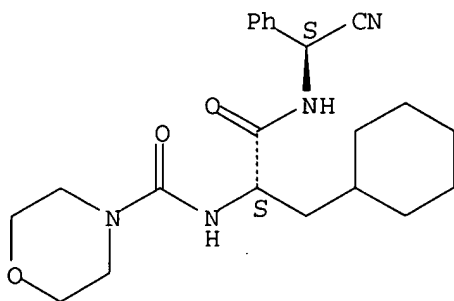
RN 479091-67-3 CAPLUS  
CN 4-Morpholinecarboxamide, N-[(1S)-2-[[[(1R)-2-[(2-chlorophenyl)methoxy]-1-cyanoethyl]amino]-1-(cyclohexylmethyl)-2-oxoethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



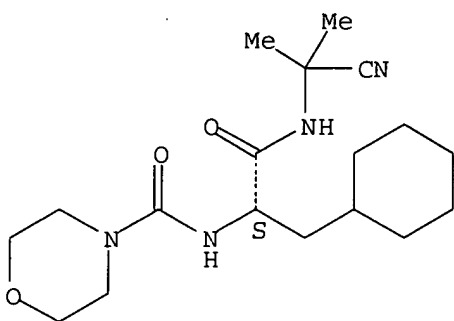
RN 479091-68-4 CAPLUS  
CN 4-Morpholinecarboxamide, N-[(1S)-2-[[[S]-cyanophenylmethyl]amino]-1-(cyclohexylmethyl)-2-oxoethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 479091-69-5 CAPLUS  
CN 4-Morpholinecarboxamide, N-[(1S)-2-[(1-cyano-1-methylethyl)amino]-1-(cyclohexylmethyl)-2-oxoethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L5 ANSWER 3 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2002:835002 CAPLUS

DOCUMENT NUMBER: 138:56234

TITLE: Design and synthesis of dipeptide nitriles as reversible and potent cathepsin S inhibitors

AUTHOR(S): Ward, Yancey D.; Thomson, David S.; Frye, Leah L.; Cywin, Charles L.; Morwick, Tina; Emmanuel, Michel J.; Zindell, Renee; McNeil, Daniel; Bekkali, Younes;

Giradot, Marc; Hrapchak, Matt; DeTuri, Molly; Crane, Kathy; White, Della; Pav, Susan; Wang, Yong; Hao, Ming-Hong; Grygon, Christine A.; Labadia, Mark E.; Freeman, Dorothy M.; Davidson, Walter; Hopkins, Jerry L.; Brown, Maryanne L.; Spero, Denice M.

CORPORATE SOURCE: Boehringer Ingelheim Pharmaceuticals, Ridgefield, CT, 06877-0368, USA

SOURCE: Journal of Medicinal Chemistry (2002), 45(25), 5471-5482

CODEN: JMCMAR; ISSN: 0022-2623

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 138:56234

AB The specificity of the immune response relies on processing of foreign proteins and presentation of antigenic peptides at the cell surface. Inhibition of antigen presentation, and the subsequent activation of T-cells, should, in theory, modulate the immune response. The cysteine protease cathepsin S performs a fundamental step in antigen presentation and therefore represents an attractive target for inhibition. Herein, the authors report a series of potent and reversible Cathepsin S inhibitors based on dipeptide nitriles. These inhibitors show nanomolar inhibition of the target enzyme as well as cellular potency in a human B cell line. The first x-ray crystal structure of a reversible inhibitor cocrystd. with cathepsin S is also reported.

IT 479091-78-6

RL: PRP (Properties)

(crystal structure of cathepsin S cocrystd. with a dipeptide nitrile as its reversible inhibitor)

RN 479091-78-6 CAPLUS

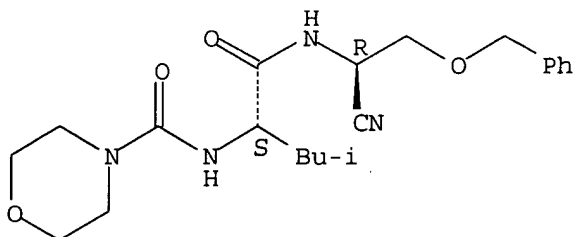
CN 4-Morpholinecarboxamide, N-[(1S)-1-[[[(1R)-1-cyano-2-(phenylmethoxy)ethyl]amino]carbonyl]-3-methylbutyl]-, compd. with cathepsin S (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 290816-77-2

CMF C21 H30 N4 O4

Absolute stereochemistry.



CM 2

CRN 71965-46-3

CMF Unspecified

CCI MAN

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

IT 290816-77-2P

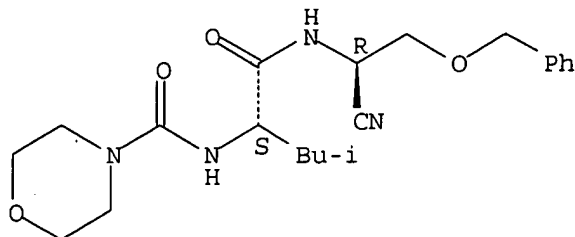
RL: BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

(preparation and biol. activity of dipeptide nitriles as reversible and potent cathepsin S inhibitors)



RN 290816-77-2 CAPLUS  
 CN 4-Morpholinecarboxamide, N-[(1S)-1-[[[(1R)-1-cyano-2-(phenylmethoxy)ethyl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 225119-70-0P 290816-49-8P 290816-76-1P  
 290816-78-3P 290816-82-9P 290816-83-0P  
 290816-89-6P 290816-91-0P 290817-01-5P  
 290817-02-6P 290817-03-7P 290817-12-8P  
 479091-50-4P 479091-51-5P 479091-52-6P  
 479091-53-7P 479091-54-8P 479091-55-9P  
 479091-56-0P 479091-57-1P 479091-58-2P  
 479091-59-3P 479091-60-6P 479091-61-7P  
 479091-62-8P 479091-63-9P 479091-64-0P  
 479091-65-1P 479091-66-2P 479091-67-3P  
 479091-68-4P 479091-69-5P

RL: BSU (Biological study, unclassified); SPN (Synthetic preparation);

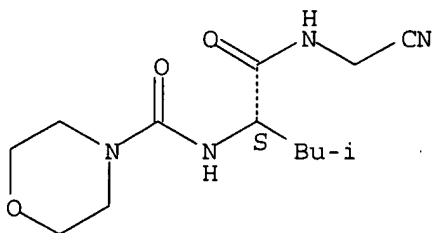
BIOL (Biological study); PREP (Preparation)

(preparation and biol. activity of dipeptide nitriles as reversible and potent cathepsin S inhibitors)

RN 225119-70-0 CAPLUS

CN 4-Morpholinecarboxamide, N-[(1S)-1-[(cyanomethyl)amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

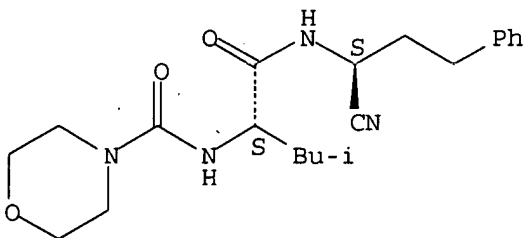
Absolute stereochemistry.



RN 290816-49-8 CAPLUS

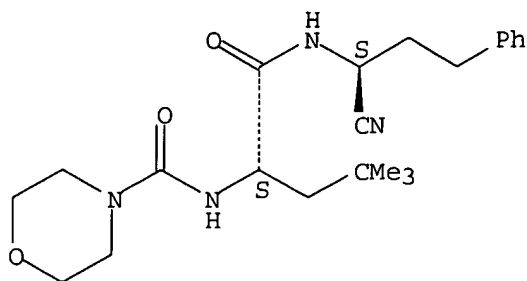
CN 4-Morpholinecarboxamide, N-[(1S)-1-[[[(1S)-1-cyano-3-phenylpropyl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



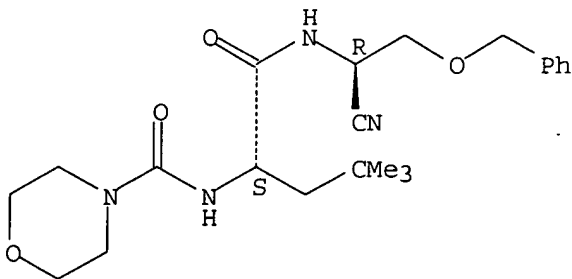
RN 290816-76-1 CAPLUS  
 CN 4-Morpholinecarboxamide, N-[(1S)-1-[[[(1S)-1-cyano-3-phenylpropyl]amino]carbonyl]-3,3-dimethylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



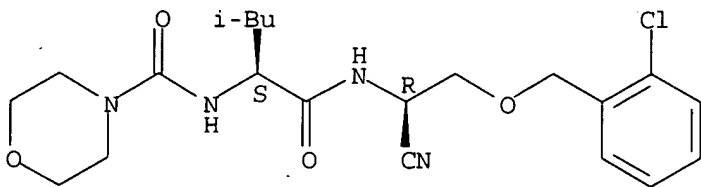
RN 290816-78-3 CAPLUS  
 CN 4-Morpholinecarboxamide, N-[(1S)-1-[[[(1R)-1-cyano-2-(phenylmethoxy)ethyl]amino]carbonyl]-3,3-dimethylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



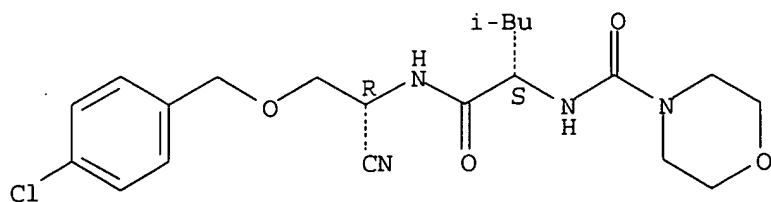
RN 290816-82-9 CAPLUS  
 CN 4-Morpholinecarboxamide, N-[(1S)-1-[[[(1R)-2-[(2-chlorophenyl)methoxy]-1-cyanoethyl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 290816-83-0 CAPLUS  
 CN 4-Morpholinecarboxamide, N-[(1S)-1-[[[(1R)-2-[(4-chlorophenyl)methoxy]-1-cyanoethyl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

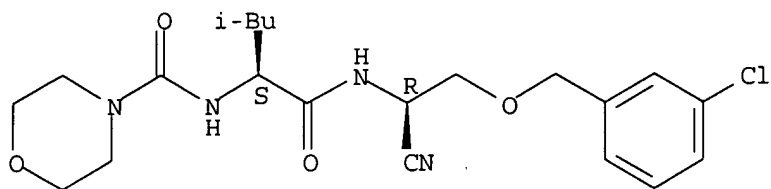
Absolute stereochemistry.



RN 290816-89-6 CAPLUS

CN 4-Morpholinecarboxamide, N-[(1S)-1-[[[(1R)-2-[(3-chlorophenyl)methoxy]-1-cyanoethyl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

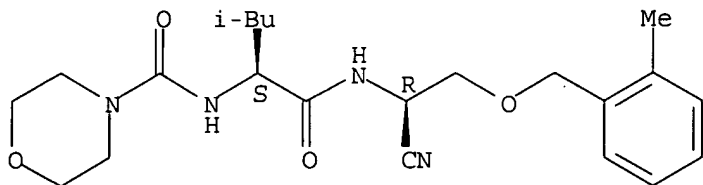
Absolute stereochemistry.



RN 290816-91-0 CAPLUS

CN 4-Morpholinecarboxamide, N-[(1S)-1-[[[(1R)-1-cyano-2-[(2-methylphenyl)methoxy]ethyl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

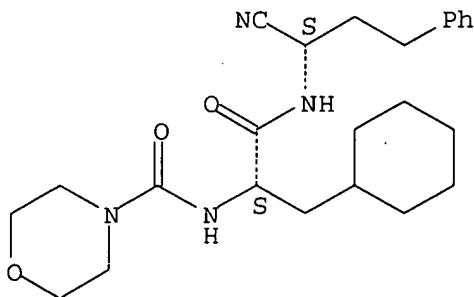
Absolute stereochemistry.



RN 290817-01-5 CAPLUS

CN 4-Morpholinecarboxamide, N-[(1S)-2-[[[(1S)-1-cyano-3-phenylpropyl]amino]-1-(cyclohexylmethyl)-2-oxoethyl]- (9CI) (CA INDEX NAME)

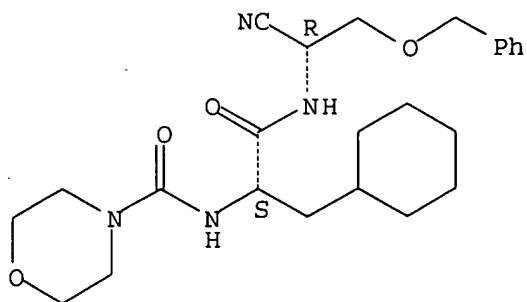
Absolute stereochemistry.



RN 290817-02-6 CAPLUS

CN 4-Morpholinecarboxamide, N-[(1S)-2-[[[(1R)-1-cyano-2-(phenylmethoxy)ethyl]amino]-1-(cyclohexylmethyl)-2-oxoethyl]- (9CI) (CA INDEX NAME)

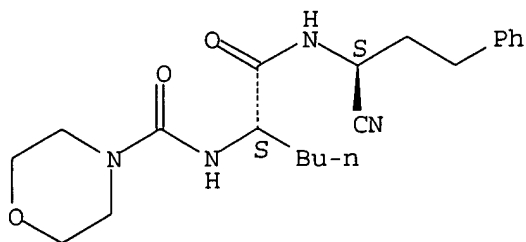
Absolute stereochemistry.



RN 290817-03-7 CAPLUS

CN 4-Morpholinecarboxamide, N-[(1S)-1-[[[(1S)-1-cyano-3-phenylpropyl]amino]carbonyl]pentyl]- (9CI) (CA INDEX NAME)

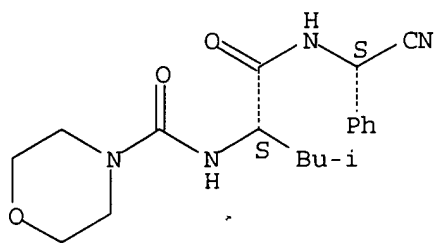
Absolute stereochemistry.



RN 290817-12-8 CAPLUS

CN 4-Morpholinecarboxamide, N-[(1S)-1-[[[(S)-cyanophenylmethyl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

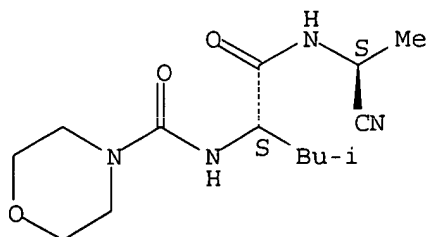
Absolute stereochemistry.



RN 479091-50-4 CAPLUS

CN 4-Morpholinecarboxamide, N-[(1S)-1-[[[(1S)-1-cyanoethyl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

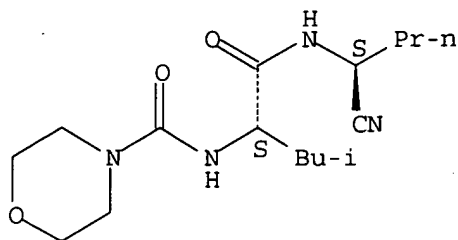


RN 479091-51-5 CAPLUS

CN 4-Morpholinecarboxamide, N-[(1S)-1-[[[(1S)-1-cyanobutyl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

methylbutyl]- (9CI) (CA INDEX NAME)

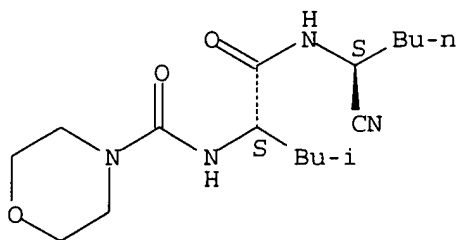
Absolute stereochemistry.



RN 479091-52-6 CAPLUS

CN 4-Morpholinecarboxamide, N-[(1S)-1-[[[(1S)-1-cyanopentyl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

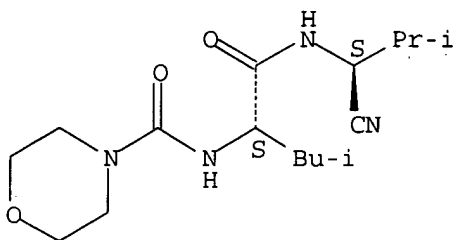
Absolute stereochemistry.



RN 479091-53-7 CAPLUS

CN 4-Morpholinecarboxamide, N-[(1S)-1-[[[(1S)-1-cyano-2-methylpropyl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

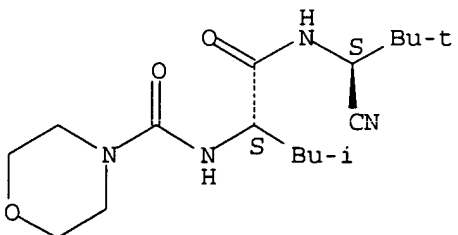
Absolute stereochemistry.



RN 479091-54-8 CAPLUS

CN 4-Morpholinecarboxamide, N-[(1S)-1-[[[(1S)-1-cyano-2,2-dimethylpropyl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

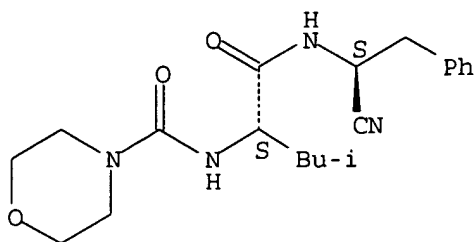


RN 479091-55-9 CAPLUS

CN 4-Morpholinecarboxamide, N-[(1S)-1-[[[(1S)-1-cyano-2-

phenylethyl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

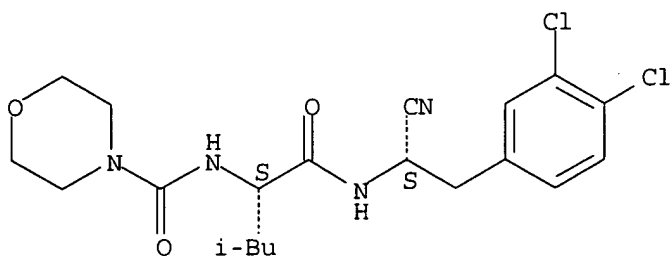
Absolute stereochemistry.



RN 479091-56-0 CAPLUS

CN 4-Morpholinecarboxamide, N-[(1S)-1-[[[(1S)-1-cyano-2-(3,4-dichlorophenyl)ethyl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

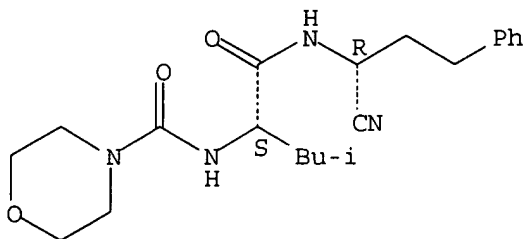
Absolute stereochemistry.



RN 479091-57-1 CAPLUS

CN 4-Morpholinecarboxamide, N-[(1S)-1-[[[(1R)-1-cyano-3-phenylpropyl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

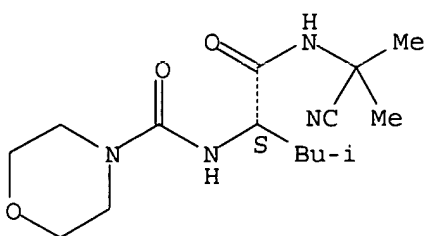
Absolute stereochemistry.



RN 479091-58-2 CAPLUS

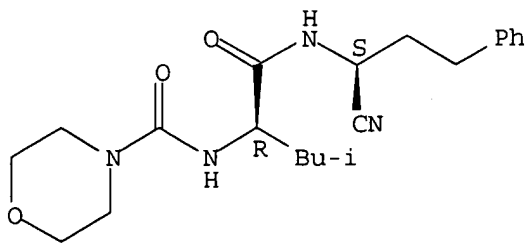
CN 4-Morpholinecarboxamide, N-[(1S)-1-[[[(1-cyano-1-methylethyl)amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



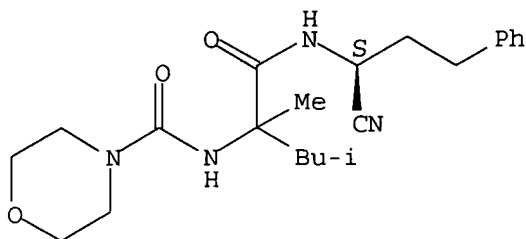
RN 479091-59-3 CAPLUS  
CN 4-Morpholinecarboxamide, N-[(1R)-1-[[[(1S)-1-cyano-3-phenylpropyl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



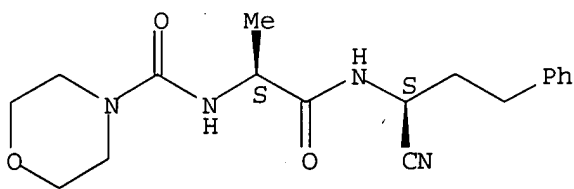
RN 479091-60-6 CAPLUS  
CN 4-Morpholinecarboxamide, N-[1-[[[(1S)-1-cyano-3-phenylpropyl]amino]carbonyl]-1,3-dimethylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



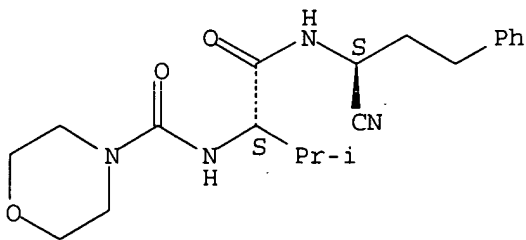
RN 479091-61-7 CAPLUS  
CN 4-Morpholinecarboxamide, N-[(1S)-2-[[[(1S)-1-cyano-3-phenylpropyl]amino]-1-methyl-2-oxoethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 479091-62-8 CAPLUS  
CN 4-Morpholinecarboxamide, N-[(1S)-1-[[[(1S)-1-cyano-3-phenylpropyl]amino]carbonyl]-2-methylpropyl]- (9CI) (CA INDEX NAME)

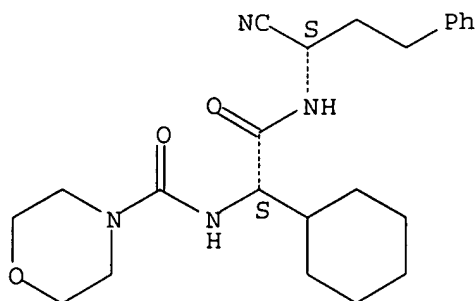
Absolute stereochemistry.



RN 479091-63-9 CAPLUS

CN 4-Morpholinecarboxamide, N-[(1S)-2-[[[(1S)-1-cyano-3-phenylpropyl]amino]-1-cyclohexyl-2-oxoethyl]- (9CI) (CA INDEX NAME)

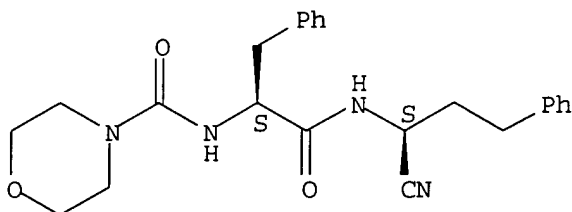
Absolute stereochemistry.



RN 479091-64-0 CAPLUS

CN 4-Morpholinecarboxamide, N-[(1S)-2-[[[(1S)-1-cyano-3-phenylpropyl]amino]-2-oxo-1-(phenylmethyl)ethyl]- (9CI) (CA INDEX NAME)

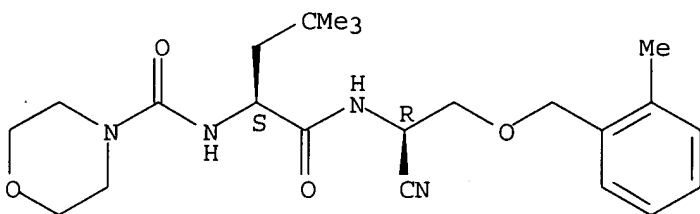
Absolute stereochemistry.



RN 479091-65-1 CAPLUS

CN 4-Morpholinecarboxamide, N-[(1S)-1-[[[(1R)-1-cyano-2-[(2-methylphenyl)methoxy]ethyl]amino]carbonyl]-3,3-dimethylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

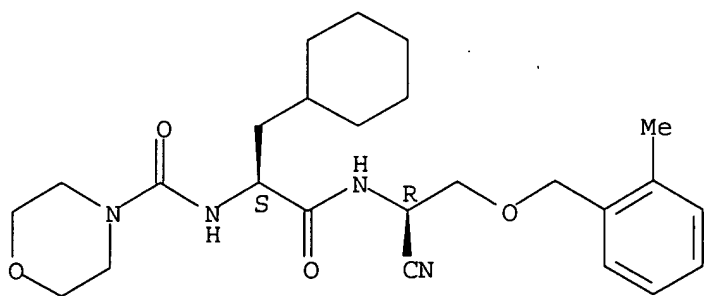


RN 479091-66-2 CAPLUS

CN 4-Morpholinecarboxamide, N-[(1S)-2-[[[(1R)-1-cyano-2-[(2-methylphenyl)methoxy]ethyl]amino]-1-(cyclohexylmethyl)-2-oxoethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

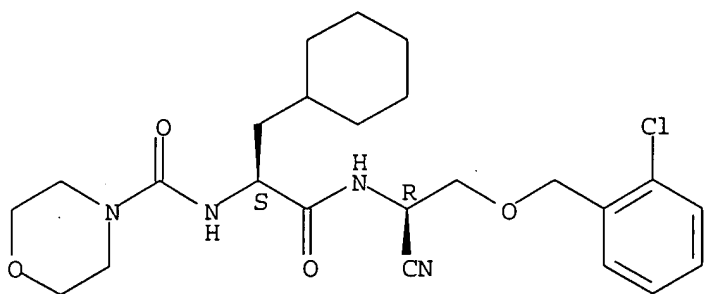




RN 479091-67-3 CAPLUS

CN 4-Morpholinecarboxamide, N-[(1S)-2-[[[(1R)-2-[(2-chlorophenyl)methoxy]-1-cyanoethyl]amino]-1-(cyclohexylmethyl)-2-oxoethyl]- (9CI) (CA INDEX NAME)

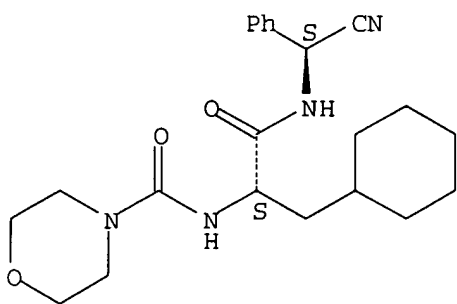
Absolute stereochemistry.



RN 479091-68-4 CAPLUS

CN 4-Morpholinecarboxamide, N-[(1S)-2-[[[(S)-cyanophenylmethyl]amino]-1-(cyclohexylmethyl)-2-oxoethyl]- (9CI) (CA INDEX NAME)

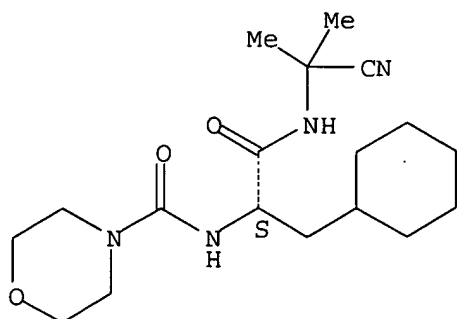
Absolute stereochemistry.



RN 479091-69-5 CAPLUS

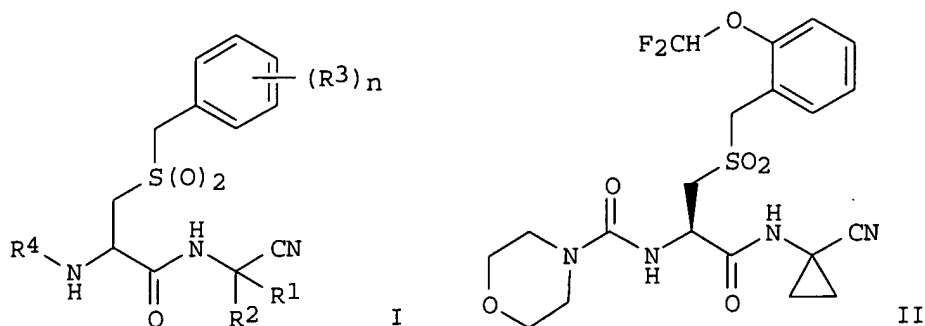
CN 4-Morpholinecarboxamide, N-[(1S)-2-[(1-cyano-1-methylethyl)amino]-1-(cyclohexylmethyl)-2-oxoethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L5 ANSWER 4 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN  
 ACCESSION NUMBER: 2001:208258 CAPLUS  
 DOCUMENT NUMBER: 134:237310  
 TITLE: Preparation and use of 2-aminoacyl-3-benzylsulfonylpropionamide derivatives as as cathepsin S inhibitors  
 INVENTOR(S): Graupe, Michael; Link, John O.; Patterson, John W.; Zipfel, Sheila  
 PATENT ASSIGNEE(S): Axys Pharmaceuticals, Inc., USA  
 SOURCE: PCT Int. Appl., 90 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 2  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001019808	A1	20010322	WO 2000-US25341	20000915
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
US 6492362	B1	20021210	US 2000-663449	20000915
US 2004014796	A1	20040122	US 2002-256354	20020927
PRIORITY APPLN. INFO.:			US 1999-154245P	P 19990916
			US 1999-171831P	P 19991222
			US 2000-224552P	P 20000810
			US 2000-663449	A3 20000915
OTHER SOURCE(S):	MARPAT 134:237310			
GI				



AB Comps. of formula I are claimed [wherein; n is 1-5, R1 is H and R2 is cyano, C5-heteroaryl or R1 and R2 are H, halo, alkyl, alkyl, X1OR5 where X1 and R5 are defined below or R1 and R2 together with the carbon atom, are (hetero)cycloalkylene; R3 is, at the first occurrence, NO2, CF3O, CHF2O, X1NR5R5, X1C(O)NR5R5, X1SR5, etc., where X1 is a bond or alkylene, R5 is H or (substituted)alkyl; R3 is at each other occurrence, is H, alkyl, CN, halo, etc.; R4 is C(O)X2R8 or S(O)2X2R8, where X2 is a bond, O or N(H or alkyl) and R8 is (substituted)alkyl, (hetero)cycloalkyl, substituted heteroaryl, etc.]. Preparation of I proceeds by one of four routes. The cyanomethyl amide side-chain may be formed by condensation of a cyanomethylamine with the parent carboxylic acid (optionally as the sulfide analog, followed by oxidation to the sulfone). The R4-NH bond may be formed by alkylation of the parent amine salt with R4L where L is a leaving group, or by addition of an amine to the corresponding isocyanate. Alternatively, the thiol-derived parent may be S-benzylated and oxidized to give compds. I. Compound II was prepared by amidation of (R)-3-[2-(difluoromethoxy)benzylsulfonyl]-2-[(1-morpholin-4-ylmethanoyl)amino]propionic acid with (1-aminocyclopropane)carbonitrile. Seventy examples of compds. I were provided. I showed Ki against cathepsin S activity in the range of 10<sup>-10</sup> to 10<sup>-7</sup> M. I inhibited cathepsin K 50-fold less than cathepsin S. Claimed uses of I are treatment of diseases which inhibition of cathepsin S can prevent.

IT 330474-09-4P 330474-81-2P 330665-93-5P

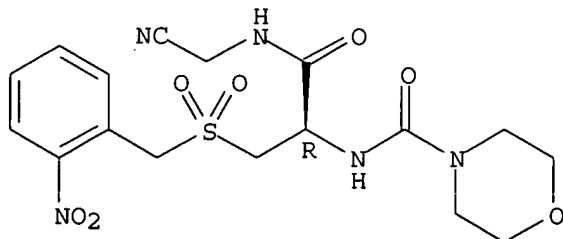
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation and use of 2-aminoacyl-3-benzylsulfonylpropionamide derivs. as selective cathepsin S inhibitors)

RN 330474-09-4 CAPLUS

CN 4-Morpholinecarboxamide, N-[(1R)-2-[(cyanomethyl)amino]-1-[[[2-(nitrophenyl)methyl]sulfonyl]methyl]-2-oxoethyl]- (9CI) (CA INDEX NAME)

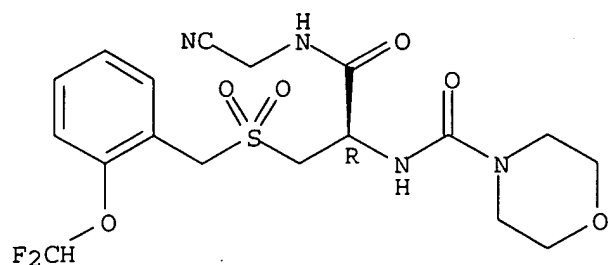
Absolute stereochemistry.



RN 330474-81-2 CAPLUS

CN 4-Morpholinecarboxamide, N-[(1R)-2-[(cyanomethyl)amino]-1-[[[2-(difluoromethoxy)phenyl]methyl]sulfonyl]methyl]-2-oxoethyl]- (9CI) (CA INDEX NAME)

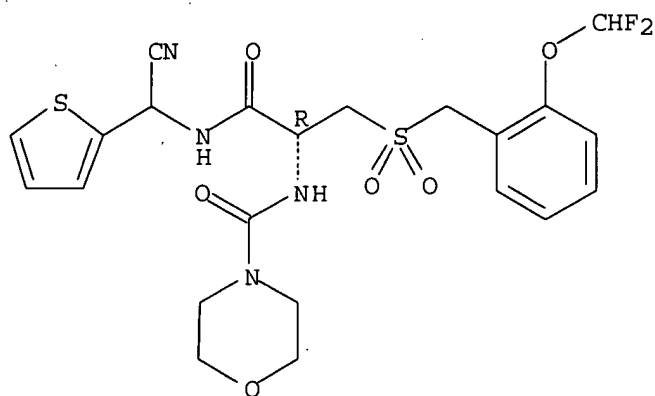
Absolute stereochemistry.



RN 330665-93-5 CAPLUS

CN 4-Morpholinecarboxamide, N-[(1R)-2-[(cyano-2-thienylmethyl)amino]-1-[[[2-(difluoromethoxy)phenyl]methyl]sulfonyl]methyl]-2-oxoethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 294642-00-5P 330475-53-1P

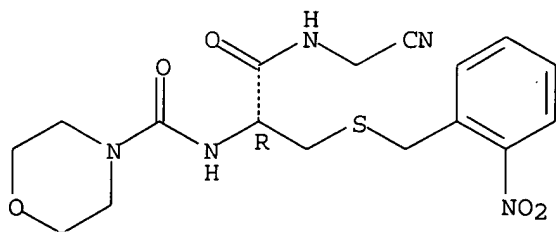
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation and use of 2-aminoacyl-3-benzylsulfonylpropionamide derivs. as selective cathepsin S inhibitors)

RN 294642-00-5 CAPLUS

CN 4-Morpholinecarboxamide, N-[(1R)-2-[(cyanomethyl)amino]-1-[[[2-nitrophenyl]methyl]thio]methyl]-2-oxoethyl]- (9CI) (CA INDEX NAME)

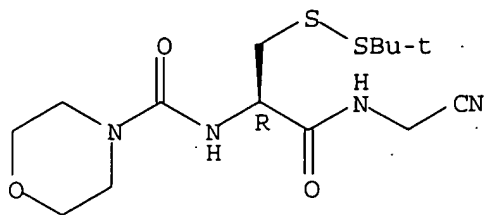
Absolute stereochemistry.



RN 330475-53-1 CAPLUS

CN 4-Morpholinecarboxamide, N-[(1R)-2-[(cyanomethyl)amino]-1-[[[2-nitrophenyl]methyl]thio]methyl]-2-oxoethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 5 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2001:208246 CAPLUS

DOCUMENT NUMBER: 134:237830

TITLE: Preparation of amino acid cyanomethyl amides as cathepsin S inhibitors

INVENTOR(S): Graupe, Michael; Link, John O.; Patterson, John W.; Zipfel, Sheila

PATENT ASSIGNEE(S): Axys Pharmaceuticals, Inc., USA

SOURCE: PCT Int. Appl., 261 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001019796	A1	20010322	WO 2000-US25415	20000915
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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2384974	AA	20010322	CA 2000-2384974	20000915
EP 1212302	A1	20020612	EP 2000-966734	20000915
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JP 2003509410	T2	20030311	JP 2001-523376	20000915
AU 777472	B2	20041021	AU 2000-77033	20000915
US 2004014796	A1	20040122	US 2002-256354	20020927
PRIORITY APPLN. INFO.:			US 1999-154245P	P 19990916
			US 1999-171831P	P 19991222
			US 2000-224552P	P 20000810
			US 2000-663449	A3 20000915
			WO 2000-US25415	W 20000915

OTHER SOURCE(S): MARPAT 134:237830

AB R4NHCH(X1SO2X2R3)CONHCR1R2CN [X1, X2 = CH2, or X1 = CH2CH2 and X2 = bond; R1 = H, R2 = cyano, heteroaryl, alkylheteroaryl, or R1, R2 = H, halo, alkyl, X3OR9; R1R2C = cycloalkylene, heterocycloalkylene; R3 = (substituted) CHR5:CHR6, CR7:NR8; R5R6 = atoms to form alkenyl, cycloalkenyl, heterocycloalkenyl, aryl, heteroaryl, etc.; R7R8 = atoms to form heterocycloalkenyl, heteroaryl, heterobicycloaryl; R4 = COX4R11, SO2X4R11; X4 = bond, O, NR12; R12 = H, alkyl; R11 = (substituted) alkyl, cycloalkylalkyl, heterocycloalkylalkyl, etc.; R9 = H, alkyl, haloalkyl; X3 = bond, alkylene], were prepared Thus, 2R-benzoylamino-3-(4-methylbenzylsulfanyl)propionic acid (preparation given), EDCI, HOBT,

aminoacetonitrile bisulfate, and N-methylmorpholine were stirred together in N-methylpyrrolidinone for 5 h to give N-[1R-cyanomethylcarbamoyl-2-(4-methylbenzylsulfanyl)ethyl]benzamide. This was stirred with oxone in MeOH for 16 h to give N-[(R)-1-(cyanomethylcarbamoyl)-2-p-tolylmethanesulfonyl]ethyl]benzamide. Title compds. inhibited cathepsin S with  $K_i$  = about  $10^{-10}$  M to  $10^{-4}$  M.

IT 330473-80-8P 330473-81-9P 330474-04-9P  
330474-09-4P 330474-26-5P 330474-81-2P  
330475-40-6P 330475-41-7P 330475-58-6P

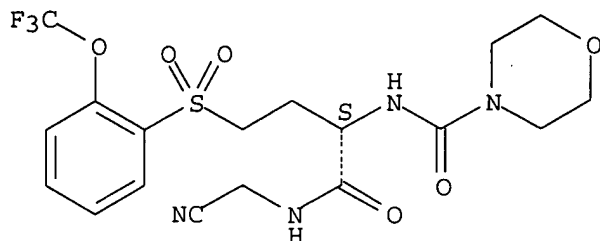
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of amino acid cyanomethyl amides as cathepsin S inhibitors)

RN 330473-80-8 CAPLUS

CN 4-Morpholinecarboxamide, N-[(1S)-1-[[[(cyanomethyl)amino]carbonyl]-3-[[2-(trifluoromethoxy)phenyl]sulfonyl]propyl]- (9CI) (CA INDEX NAME)

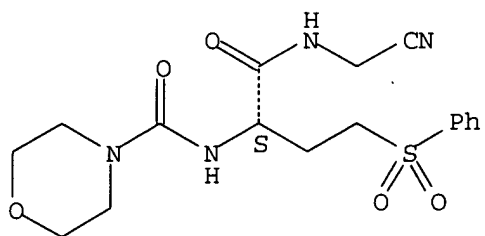
Absolute stereochemistry.



RN 330473-81-9 CAPLUS

CN 4-Morpholinecarboxamide, N-[(1S)-1-[[[(cyanomethyl)amino]carbonyl]-3-(phenylsulfonyl)propyl]- (9CI) (CA INDEX NAME)

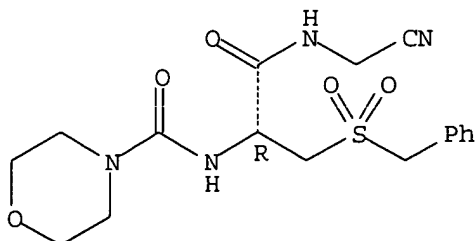
Absolute stereochemistry.



RN 330474-04-9 CAPLUS

CN 4-Morpholinecarboxamide, N-[(1R)-2-[(cyanomethyl)amino]-2-oxo-1-[[[(phenylmethyl)sulfonyl]methyl]ethyl]- (9CI) (CA INDEX NAME)

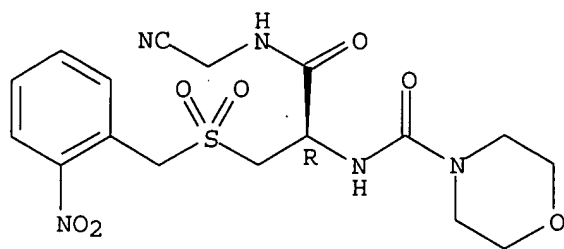
Absolute stereochemistry.



RN 330474-09-4 CAPLUS

CN 4-Morpholinecarboxamide, N-[(1R)-2-[(cyanomethyl)amino]-1-[[[(2-nitrophenyl)methyl]sulfonyl]methyl]-2-oxoethyl]- (9CI) (CA INDEX NAME)

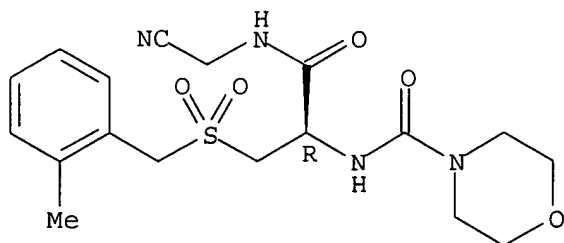
Absolute stereochemistry.



RN 330474-26-5 CAPLUS

CN 4-Morpholinecarboxamide, N-[(1R)-2-[(cyanomethyl)amino]-1-[[[(2-methylphenyl)methyl]sulfonyl]methyl]-2-oxoethyl]- (9CI) (CA INDEX NAME)

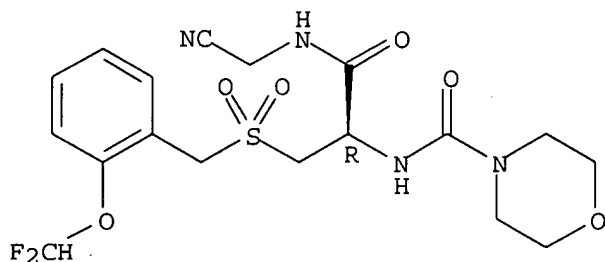
Absolute stereochemistry.



RN 330474-81-2 CAPLUS

CN 4-Morpholinecarboxamide, N-[(1R)-2-[(cyanomethyl)amino]-1-[[[(2-(difluoromethoxy)phenyl)methyl]sulfonyl]methyl]-2-oxoethyl]- (9CI) (CA INDEX NAME)

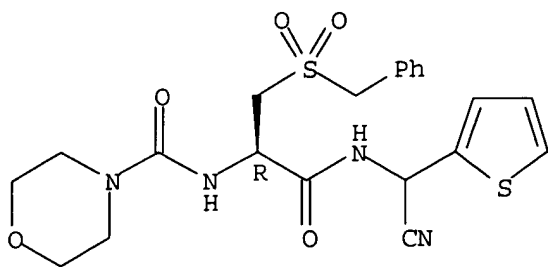
Absolute stereochemistry.



RN 330475-40-6 CAPLUS

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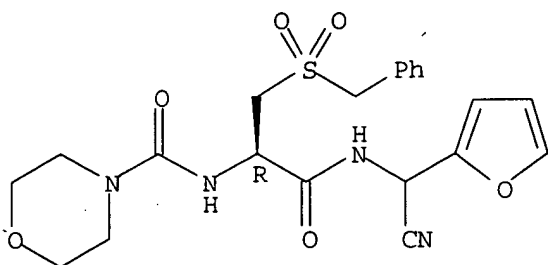
Absolute stereochemistry.



RN 330475-41-7 CAPLUS

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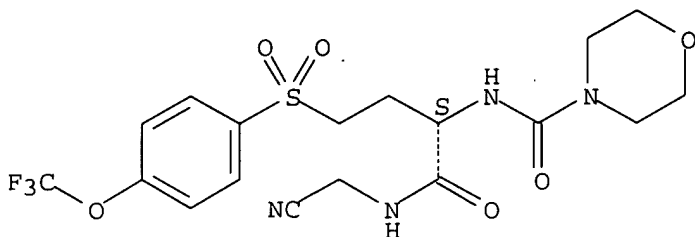
Absolute stereochemistry.



RN 330475-58-6 CAPLUS

CN 4-Morpholinecarboxamide, N-[(1S)-1-[[[cyanomethyl]amino]carbonyl]-3-[[4-(trifluoromethoxy)phenyl]sulfonyl]propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 294641-09-1P 294642-00-5P 330475-53-1P

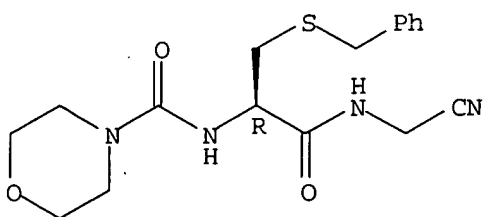
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of amino acid cyanomethyl amides as cathepsin S inhibitors)

RN 294641-09-1 CAPLUS

CN 4-Morpholinecarboxamide, N-[(1R)-2-[(cyanomethyl)amino]-2-oxo-1-[[phenylmethyl]thio]methyl]ethyl]- (9CI) (CA INDEX NAME)

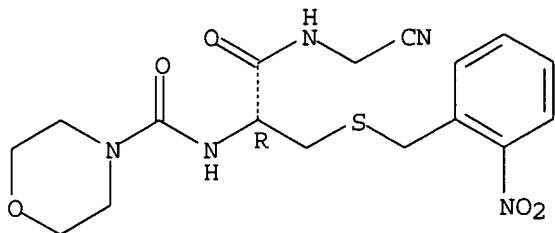
Absolute stereochemistry.





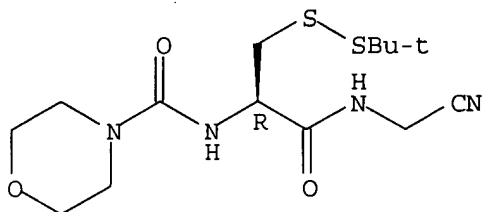
RN 294642-00-5 CAPLUS  
 CN 4-Morpholinecarboxamide, N-[(1R)-2-[(cyanomethyl)amino]-1-[[[(2-nitrophenyl)methyl]thio]methyl]-2-oxoethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 330475-53-1 CAPLUS  
 CN 4-Morpholinecarboxamide, N-[(1R)-2-[(cyanomethyl)amino]-1-[[[(1,1-dimethylethyl)dithio]methyl]-2-oxoethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 6 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN  
 ACCESSION NUMBER: 2000:666700 CAPLUS  
 DOCUMENT NUMBER: 133:252170  
 TITLE: Preparation of novel N-cyanomethyl amides as protease inhibitors  
 INVENTOR(S): Bryant, Clifford M.; Bunin, Barry A.; Kraynack, Erica A.; Patterson, John W.  
 PATENT ASSIGNEE(S): Axys Pharmaceuticals, Inc., USA  
 SOURCE: PCT Int. Appl., 137 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 2  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000055125	A2	20000921	WO 2000-US6747	20000315
WO 2000055125	A3	20010426		

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RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

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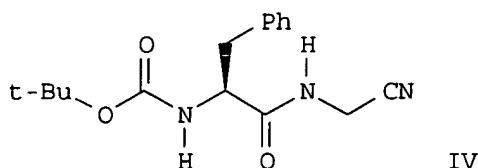
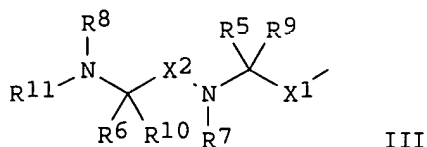
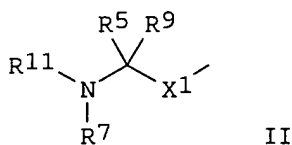
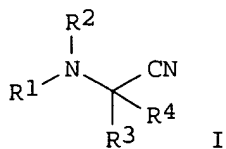
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PRIORITY APPLN. INFO.:

US 1999-124420P	P	19990315
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US 2000-526090	A1	20000315
US 2000-526485	A3	20000315
WO 2000-US6747	W	20000315
US 2002-205600	B1	20020724

OTHER SOURCE(S): MARPAT 133:252170

GI



AB The title compds. [I; R1 = II, III (wherein X1, X2 = CO, CH2SO2; R5, R6 =

H, alkyl; R7, R8 = H, alkyl, etc.; R9, R10 = alkyl optionally substituted with CN, halo, NO2, etc.; R11 = X5X6R18; X5 = CO, COCO, SO2; X6 = a bond, O, NH, N(alkyl); R18 = alkyl optionally substituted with CN, halo, NO2, etc.); R2 = H, alkyl, etc.; R3 = H, alkyl, etc.; R4 = H, alkyl optionally substituted with CN, halo, NO2, etc.; R4 and R2 taken together form trimethylene, tetramethylene, phenylene-1,2-dimethylene, optionally substituted with hydroxy, oxo or methylene; R4 and R3 together with the carbon atom to which both are attached form cycloalkylene, heterocycloalkylene], useful for treating diseases associated with cysteine protease activity, particularly diseases associated with activity of cathepsins B, K, L or S such as inflammation and asthma, were prepared and formulated. Thus, reacting 2(S)-tert-butoxycarbonylamino-3-phenylpropionic acid with aminoacetonitrile.HCl in the presence of Et3N in DMF and MeCN afforded the amide (1S)-IV. Biol. data for compds. I were given.

IT 225120-04-7P 294641-09-1P 294641-99-9P

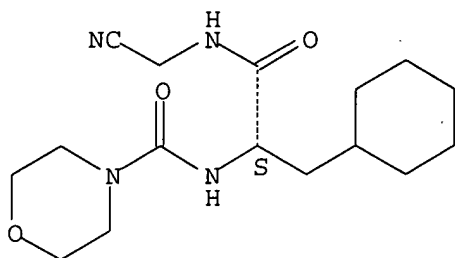
294642-00-5P 294642-01-6P 294642-15-2P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(preparation of novel N-cyanomethyl amides as protease inhibitors)

RN 225120-04-7 CAPLUS

CN 4-Morpholinecarboxamide, N-[(1S)-2-[(cyanomethyl)amino]-1-(cyclohexylmethyl)-2-oxoethyl]- (9CI) (CA INDEX NAME)

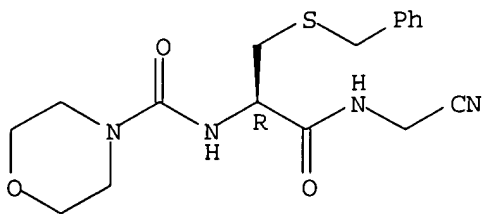
Absolute stereochemistry.



RN 294641-09-1 CAPLUS

CN 4-Morpholinecarboxamide, N-[(1R)-2-[(cyanomethyl)amino]-2-oxo-1-[[[(phenylmethyl)thio]methyl]ethyl]- (9CI) (CA INDEX NAME)

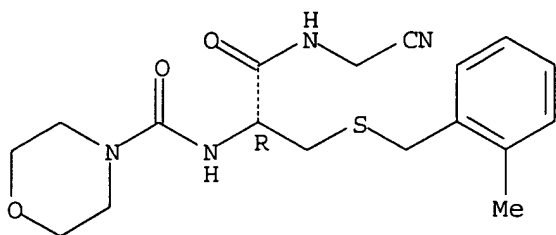
Absolute stereochemistry.



RN 294641-99-9 CAPLUS

CN 4-Morpholinecarboxamide, N-[(1R)-2-[(cyanomethyl)amino]-1-[[[(2-methylphenyl)methyl]thio]methyl]-2-oxoethyl]- (9CI) (CA INDEX NAME)

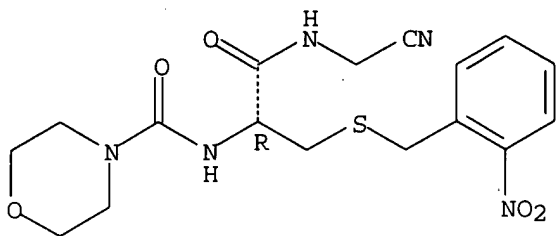
Absolute stereochemistry.



RN 294642-00-5 CAPLUS

CN 4-Morpholinecarboxamide, N-[(1R)-2-[(cyanomethyl)amino]-1-[[[(2-nitrophenyl)methyl]thio]methyl]-2-oxoethyl]- (9CI) (CA INDEX NAME)

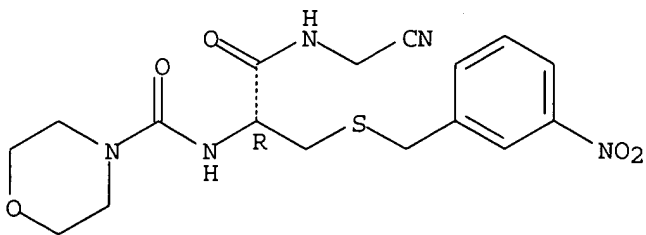
Absolute stereochemistry.



RN 294642-01-6 CAPLUS

CN 4-Morpholinecarboxamide, N-[(1R)-2-[(cyanomethyl)amino]-1-[[[(3-nitrophenyl)methyl]thio]methyl]-2-oxoethyl]- (9CI) (CA INDEX NAME)

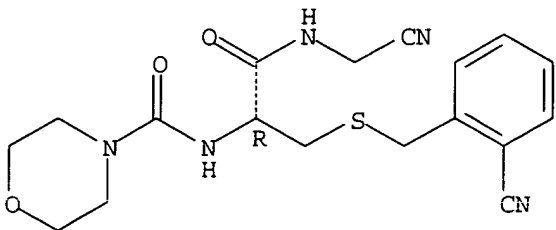
Absolute stereochemistry.



RN 294642-15-2 CAPLUS

CN 4-Morpholinecarboxamide, N-[(1R)-2-[(cyanomethyl)amino]-1-[[[(2-cyanophenyl)methyl]thio]methyl]-2-oxoethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. °



L5 ANSWER 7 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2000:628128 CAPLUS

DOCUMENT NUMBER: 133:208196

TITLE: Preparation of peptides as reversible inhibitors of

cathepsin S  
 INVENTOR(S): Cywin, Charles L.; Frye, Leah L.; Morwick, Tina;  
 Spero, Denise M.; Thomson, David; Ward, Yancey  
 PATENT ASSIGNEE(S): Boehringer Ingelheim Pharmaceuticals, Inc., USA  
 SOURCE: PCT Int. Appl., 315 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000051998	A1	20000908	WO 1999-US26278	19991105
W: CA, JP, MX RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2360740	AA	20000908	CA 1999-2360740	19991105
EP 1159273	A1	20011205	EP 1999-973745	19991105
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
US 6395897	B1	20020528	US 1999-434106	19991105
JP 2002538151	T2	20021112	JP 2000-602225	19991105
US 6608057	B2	20030819	US 2001-82952	20011024
US 2002091259	A1	20020711	US 2002-82952	20020224
US 2003158406	A1	20030821	US 2003-366282	20030213
US 6730671	B2	20040504		
PRIORITY APPLN. INFO.:			US 1999-122570P	P 19990302
			US 1999-434106	A1 19991105
			WO 1999-US26278	W 19991105
			US 2001-82952	A3 20011024

OTHER SOURCE(S): MARPAT 133:208196

AB Comps. R1-A-NHCR2R3C(:X)NR4CR5R6R7 [A = C:O, C:S, C:NH or substituted imino group; R1 = (un)substituted alkyl, cycloalkyl, aryl, heterocyclyl, heteroaryl, amino; R2, R4 = H, alkyl; R3, R6 = H or (un)substituted alkyl, cycloalkyl, aryl, heterocyclyl, heteroaryl; R5 = H, alkyl, cycloalkyl; R7 = R8C(Z), where Z = O, S, NH or substituted derivative and R8 is (un)substituted 5-8 membered monocyclic or 8-11 membered bicyclic heteroaryl having 1-4 heteroatoms selected from N, O and S; X = O, S, NOH] were prepared as cathepsin S inhibitors. Thus, morpholine-4-carboxylic acid [1-(S)-[1-(S)-cyano-3-phenylpropylcarbonyl]-3-methylbutyl]amide was prepared by coupling L-homophenylalaninamide with N-(4-morpholinecarbonyl)-L-leucine and reaction with cyanuric chloride. Comps. of the invention were evaluated for inhibition of cathepsin S (IC50 ≤ 100 μM).

IT 290816-49-8P 290816-76-1P 290816-77-2P  
 290816-78-3P 290816-79-4P 290816-81-8P  
 290816-82-9P 290816-83-0P 290816-84-1P  
 290816-85-2P 290816-86-3P 290816-87-4P  
 290816-88-5P 290816-89-6P 290816-91-0P  
 290816-92-1P 290816-93-2P 290816-94-3P  
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 290817-07-1P 290817-08-2P 290817-10-6P  
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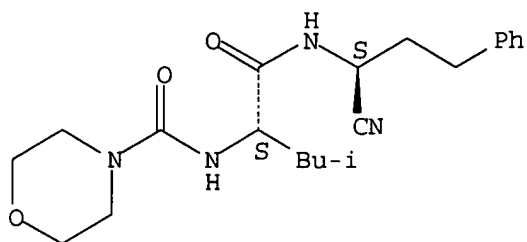
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of peptides as reversible inhibitors of cathepsin S)

RN 290816-49-8 CAPLUS

CN 4-Morpholinecarboxamide, N-[(1S)-1-[[[(1S)-1-cyano-3-phenylpropyl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

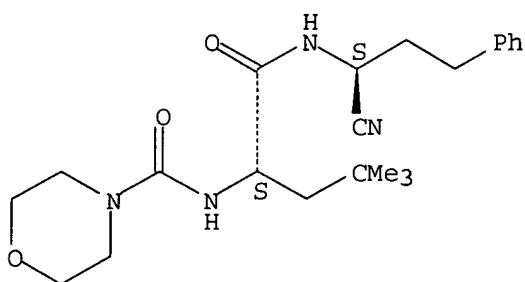
Absolute stereochemistry.



RN 290816-76-1 CAPLUS

CN 4-Morpholinecarboxamide, N-[(1S)-1-[[[(1S)-1-cyano-3-phenylpropyl]amino]carbonyl]-3,3-dimethylbutyl]- (9CI) (CA INDEX NAME)

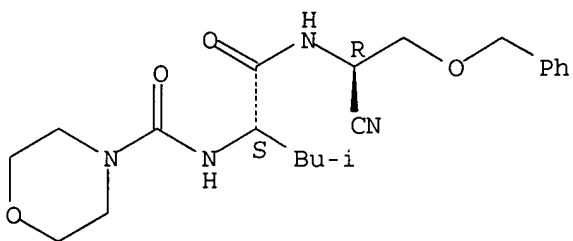
Absolute stereochemistry.



RN 290816-77-2 CAPLUS

CN 4-Morpholinecarboxamide, N-[(1S)-1-[[[(1R)-1-cyano-2-(phenylmethoxy)ethyl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

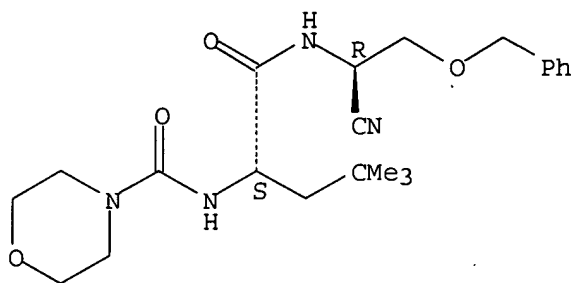
Absolute stereochemistry.



RN 290816-78-3 CAPLUS

CN 4-Morpholinecarboxamide, N-[(1S)-1-[[[(1R)-1-cyano-2-(phenylmethoxy)ethyl]amino]carbonyl]-3,3-dimethylbutyl]- (9CI) (CA INDEX NAME)

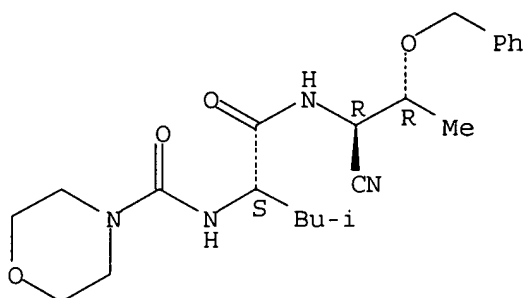
Absolute stereochemistry.



RN 290816-79-4 CAPLUS

CN 4-Morpholinecarboxamide, N-[(1S)-1-[[[(1R,2R)-1-cyano-2-(phenylmethoxy)propyl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

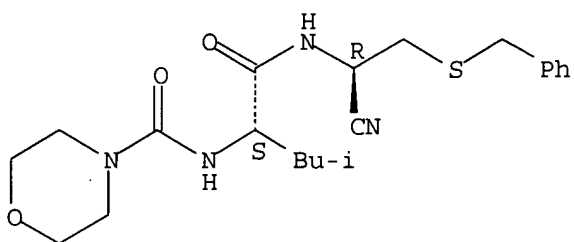
Absolute stereochemistry.



RN 290816-81-8 CAPLUS

CN 4-Morpholinecarboxamide, N-[(1S)-1-[[[(1R)-1-cyano-2-(phenylmethoxy)propyl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

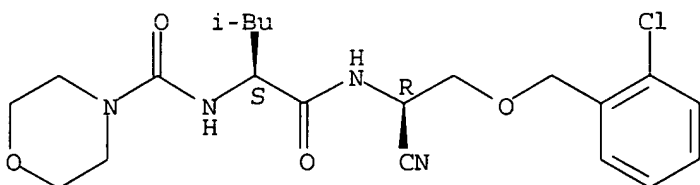
Absolute stereochemistry.



RN 290816-82-9 CAPLUS

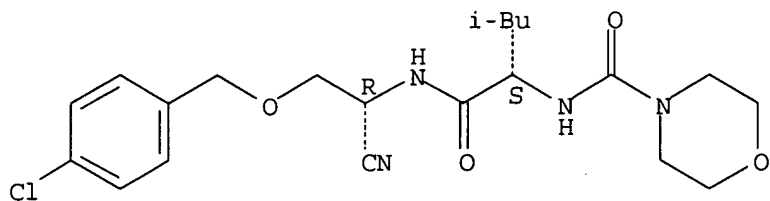
CN 4-Morpholinecarboxamide, N-[(1S)-1-[[[(1R)-2-[(2-chlorophenyl)methoxy]-1-cyanoethyl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



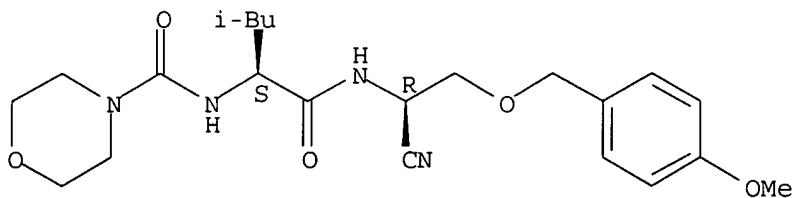
RN 290816-83-0 CAPLUS  
 CN 4-Morpholinecarboxamide, N-[(1S)-1-[[[(1R)-2-[(4-chlorophenyl)methoxy]-1-cyanoethyl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



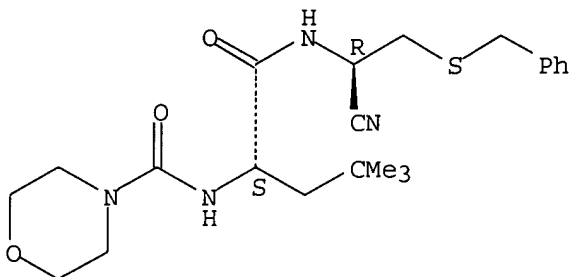
RN 290816-84-1 CAPLUS  
 CN 4-Morpholinecarboxamide, N-[(1S)-1-[[[(1R)-1-cyano-2-[(4-methoxyphenyl)methoxy]ethyl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 290816-85-2 CAPLUS  
 CN 4-Morpholinecarboxamide, N-[(1S)-1-[[[(1R)-1-cyano-2-[(phenylmethyl)thio]ethyl]amino]carbonyl]-3,3-dimethylbutyl]- (9CI) (CA INDEX NAME)

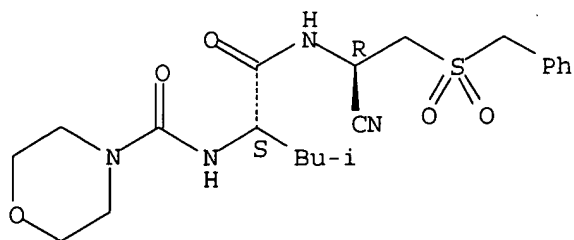
Absolute stereochemistry.



RN 290816-86-3 CAPLUS  
 CN 4-Morpholinecarboxamide, N-[(1S)-1-[[[(1R)-1-cyano-2-[(phenylmethyl)sulfonyl]ethyl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

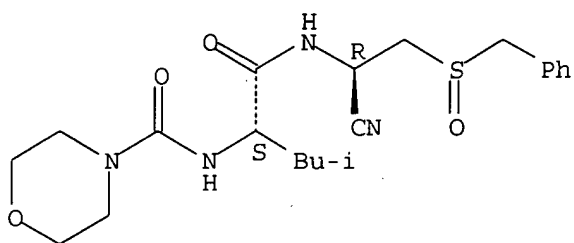




RN 290816-87-4 CAPLUS

CN 4-Morpholinecarboxamide, N-[(1S)-1-[[[(1R)-1-cyano-2-[(phenylmethyl) sulfinyl]ethyl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

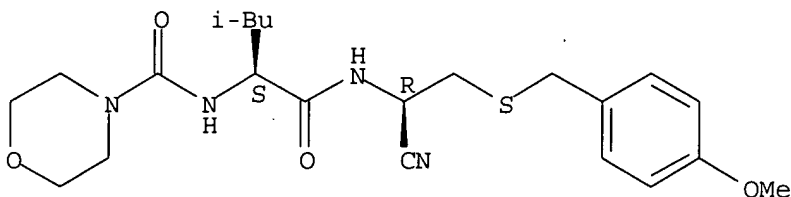
Absolute stereochemistry.



RN 290816-88-5 CAPLUS

CN 4-Morpholinecarboxamide, N-[(1S)-1-[[[(1R)-1-cyano-2-[(4-methoxyphenyl)methyl]thio]ethyl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

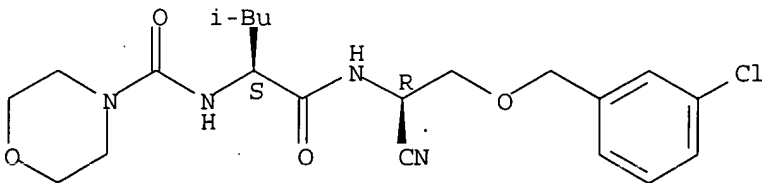
Absolute stereochemistry.



RN 290816-89-6 CAPLUS

CN 4-Morpholinecarboxamide, N-[(1S)-1-[[[(1R)-2-[(3-chlorophenyl)methoxy]ethyl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

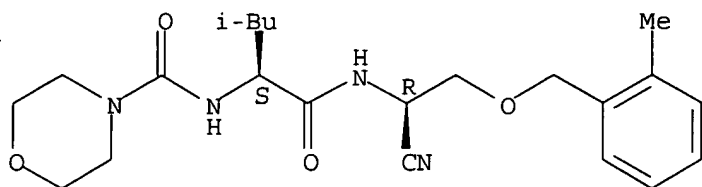
Absolute stereochemistry.



RN 290816-91-0 CAPLUS

CN 4-Morpholinecarboxamide, N-[(1S)-1-[[[(1R)-1-cyano-2-[(2-methylphenyl)methoxy]ethyl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

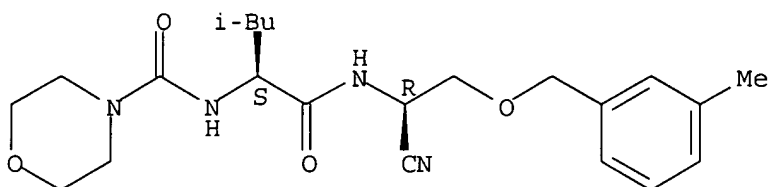
Absolute stereochemistry.



RN 290816-92-1 CAPLUS

CN 4-Morpholinecarboxamide, N-[(1S)-1-[[[(1R)-1-cyano-2-[(3-methylphenyl)methoxy]ethyl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

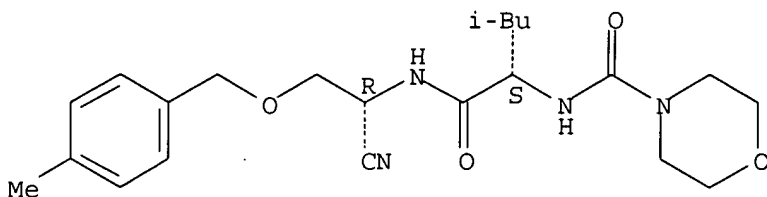
Absolute stereochemistry.



RN 290816-93-2 CAPLUS

CN 4-Morpholinecarboxamide, N-[(1S)-1-[[[(1R)-1-cyano-2-[(4-methylphenyl)methoxy]ethyl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

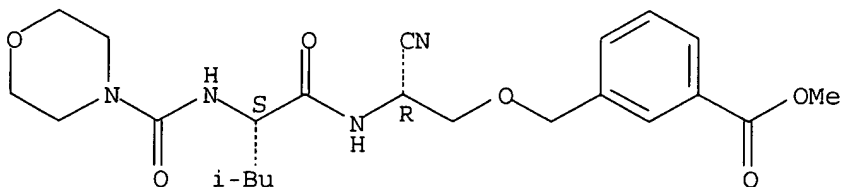
Absolute stereochemistry.



RN 290816-94-3 CAPLUS

CN Benzoic acid, 3-[[[(2R)-2-cyano-2-[[[(2S)-4-methyl-2-[(4-morpholinylcarbonyl)amino]-1-oxopentyl]amino]ethoxy]methyl]-, methyl ester (9CI) (CA INDEX NAME)

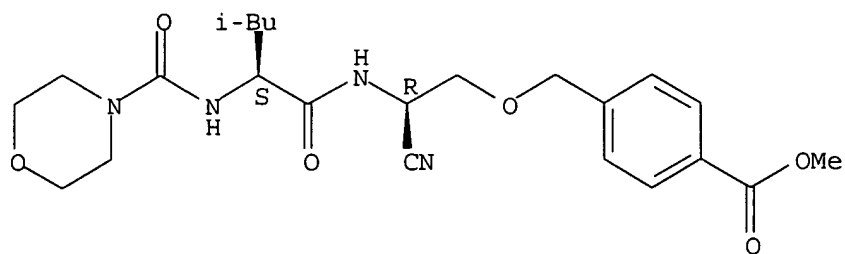
Absolute stereochemistry.



RN 290816-95-4 CAPLUS

CN Benzoic acid, 4-[[[(2R)-2-cyano-2-[[[(2S)-4-methyl-2-[(4-morpholinylcarbonyl)amino]-1-oxopentyl]amino]ethoxy]methyl]-, methyl ester (9CI) (CA INDEX NAME)

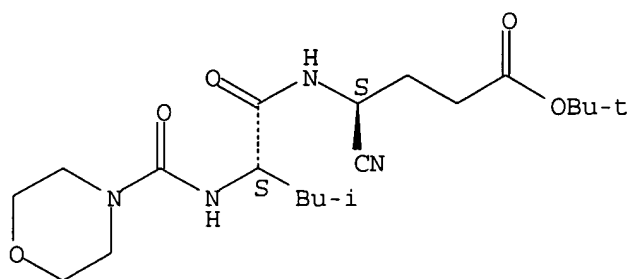
Absolute stereochemistry.



RN 290816-96-5 CAPLUS

CN Butanoic acid, 4-cyano-4-[[[(2S)-4-methyl-2-[(4-morpholinylcarbonyl)amino]-1-oxopentyl]amino]-, 1,1-dimethylethyl ester, (4S)- (9CI) (CA INDEX NAME)

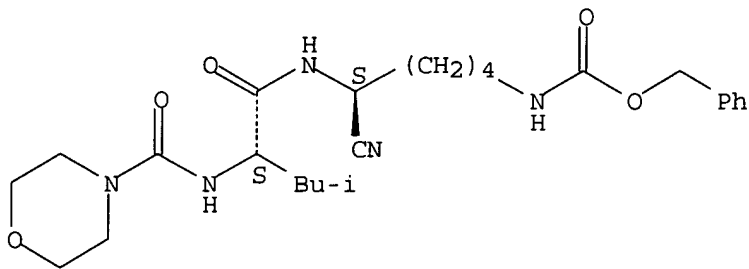
Absolute stereochemistry.



RN 290816-97-6 CAPLUS

CN Carbamic acid, [(5S)-5-cyano-5-[[[(2S)-4-methyl-2-[(4-morpholinylcarbonyl)amino]-1-oxopentyl]amino]pentyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

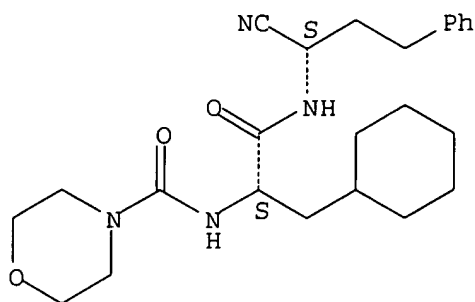
Absolute stereochemistry.



RN 290817-01-5 CAPLUS

CN 4-Morpholinecarboxamide, N-[(1S)-2-[[[(1S)-1-cyano-3-phenylpropyl]amino]-1-(cyclohexylmethyl)-2-oxoethyl]- (9CI) (CA INDEX NAME)

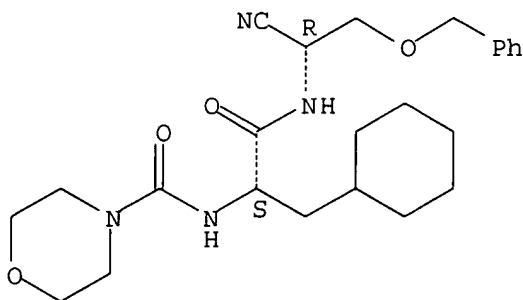
Absolute stereochemistry.



RN 290817-02-6 CAPLUS

CN 4-Morpholinecarboxamide, N-[(1S)-2-[[[(1R)-1-cyano-2-(phenylmethoxy)ethyl]amino]-1-(cyclohexylmethyl)-2-oxoethyl]- (9CI) (CA INDEX NAME)

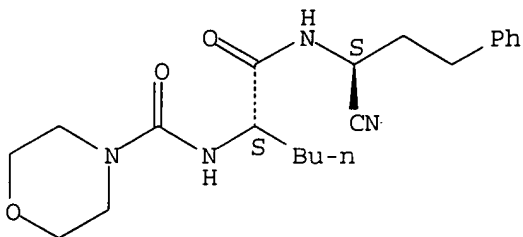
Absolute stereochemistry.



RN 290817-03-7 CAPLUS

CN 4-Morpholinecarboxamide, N-[(1S)-1-[[[(1S)-1-cyano-3-phenylpropyl]amino]carbonyl]pentyl]- (9CI) (CA INDEX NAME)

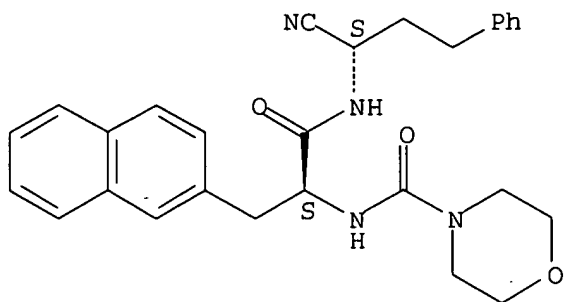
Absolute stereochemistry.



RN 290817-07-1 CAPLUS

CN 4-Morpholinecarboxamide, N-[(1S)-2-[[[(1S)-1-cyano-3-phenylpropyl]amino]-1-(2-naphthalenylmethyl)-2-oxoethyl]- (9CI) (CA INDEX NAME)

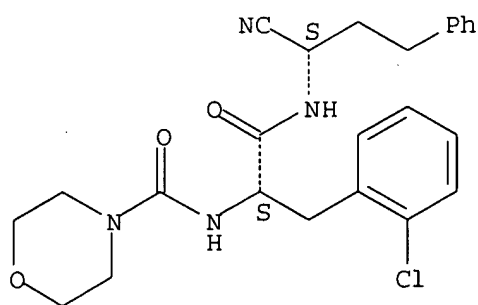
Absolute stereochemistry.



RN 290817-08-2 CAPLUS

CN 4-Morpholinecarboxamide, N-[(1S)-1-[(2-chlorophenyl)methyl]-2-[[[(1S)-1-cyano-3-phenylpropyl]amino]-2-oxoethyl]- (9CI) (CA INDEX NAME)

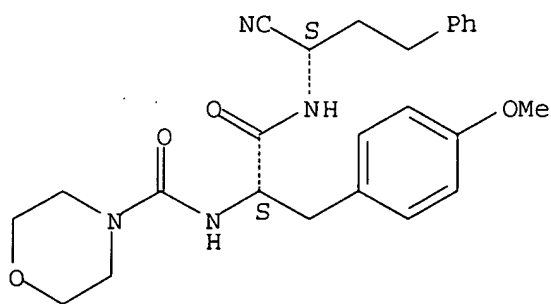
Absolute stereochemistry.



RN 290817-10-6 CAPLUS

CN 4-Morpholinecarboxamide, N-[(1S)-2-[[[(1S)-1-cyano-3-phenylpropyl]amino]-1-[(4-methoxyphenyl)methyl]-2-oxoethyl]- (9CI) (CA INDEX NAME)

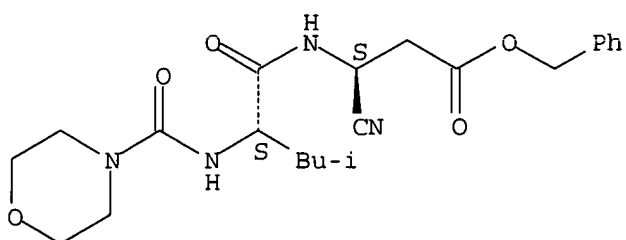
Absolute stereochemistry.



RN 290817-11-7 CAPLUS

CN Propanoic acid, 3-cyano-3-[[[(2S)-4-methyl-2-[(4-morpholinylcarbonyl)amino]-1-oxopentyl]amino]-, phenylmethyl ester, (3S)- (9CI) (CA INDEX NAME)

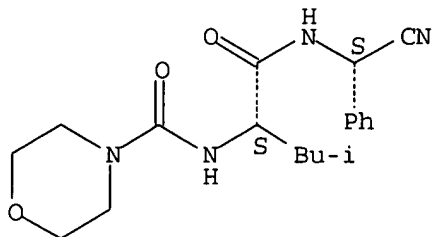
Absolute stereochemistry.



RN 290817-12-8 CAPLUS

CN 4-Morpholinecarboxamide, N-[(1S)-1-[[[(S)-cyanophenylmethyl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

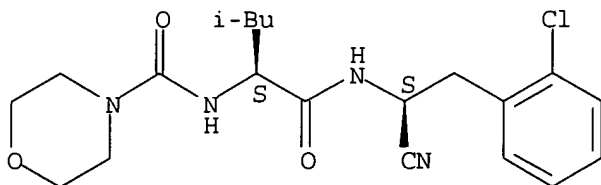
Absolute stereochemistry.



RN 290817-14-0 CAPLUS

CN 4-Morpholinecarboxamide, N-[(1S)-1-[[[(1S)-2-(2-chlorophenyl)-1-cyanoethyl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

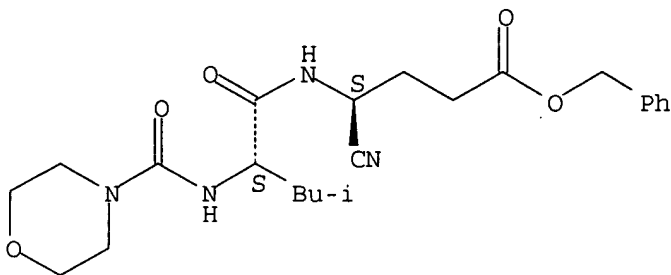
Absolute stereochemistry.



RN 290817-15-1 CAPLUS

CN Butanoic acid, 4-cyano-4-[[[(2S)-4-methyl-2-[(4-morpholinylcarbonyl)amino]-1-oxopentyl]amino]-, phenylmethyl ester, (4S)- (9CI) (CA INDEX NAME)

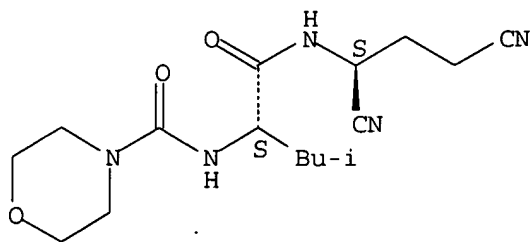
Absolute stereochemistry.



RN 290817-17-3 CAPLUS

CN 4-Morpholinecarboxamide, N-[(1S)-1-[[[(1S)-1,3-dicyanopropyl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

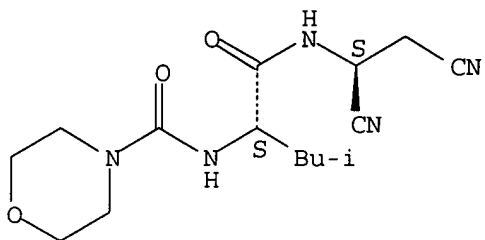
Absolute stereochemistry.



RN 290817-18-4 CAPLUS

CN 4-Morpholinecarboxamide, N-[(1S)-1-[[[(1S)-1,2-dicyanoethyl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

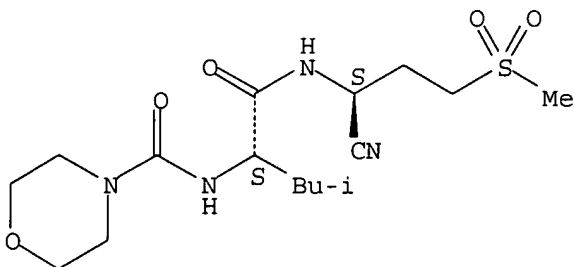
Absolute stereochemistry.



RN 290817-19-5 CAPLUS

CN 4-Morpholinecarboxamide, N-[(1S)-1-[[[(1S)-1-cyano-3-(methylsulfonyl)propyl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

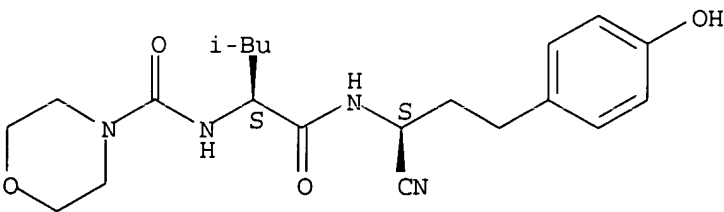
Absolute stereochemistry.



RN 290817-20-8 CAPLUS

CN 4-Morpholinecarboxamide, N-[(1S)-1-[[[(1S)-1-cyano-3-(4-hydroxyphenyl)propyl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

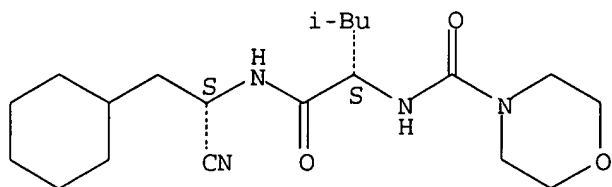


RN 290817-21-9 CAPLUS

CN 4-Morpholinecarboxamide, N-[(1S)-1-[[[(1S)-1-cyano-2-

cyclohexylethyl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 8 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN  
ACCESSION NUMBER: 2000:592709 CAPLUS  
DOCUMENT NUMBER: 133:193494  
TITLE: Preparation of di- and tripeptide nitrile derivatives as inhibitors of cathepsin L and cathepsin S  
INVENTOR(S): Tucker, Howard; Large, Michael Stewart; Oldfield, John; Johnstone, Craig; Edwards, Philip Neil  
PATENT ASSIGNEE(S): Astrazeneca AB, Swed.  
SOURCE: PCT Int. Appl., 83 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000049008	A1	20000824	WO 2000-GB529	20000216
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1155011	A1	20011121	EP 2000-903845	20000216
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002537294	T2	20021105	JP 2000-599748	20000216
PRIORITY APPLN. INFO.:				
			GB 1999-3853	A 19990220
			GB 1999-16099	A 19990710
			GB 1999-17171	A 19990723
			WO 2000-GB529	W 20000216

OTHER SOURCE(S): MARPAT 133:193494

AB Peptide nitriles R1-(AA1)n-AA2-NHCR2R3CN [n = 0 or 1; R1 = H, (un)substituted benzyl or acyl; R2 = H, (un)substituted alkyl, alkoxy, alkenyl, alkynyl, alkoxy carbonyl, carbamoyl, Ph, etc.; R3 = H, alkyl; AA1 and AA2 are certain amino acid residues] were prepared as cathepsin L or cathepsin S inhibitors. Thus, Cbz-Leu-Phe-NHCH(SPr-i)CN (Cbz = benzyloxycarbonyl), prepared by treating the amide with trifluoroacetic anhydride, showed IC50 = 38 nM for inhibition of cathepsin L.

IT 289062-09-5P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(preparation of di- and tripeptide nitrile derivs. as inhibitors of

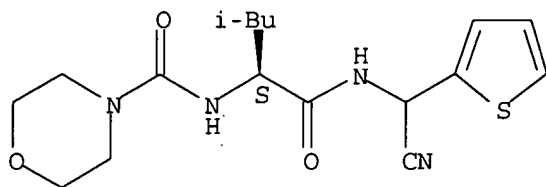


cathepsin L and cathepsin S)

RN 289062-09-5 CAPLUS

CN 4-Morpholinecarboxamide, N-[(1S)-1-[[[(cyano-2-thienylmethyl)amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 9 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1999:325961 CAPLUS

DOCUMENT NUMBER: 130:352553

TITLE: Synthesis of dipeptide nitriles as inhibitors of cysteine cathepsins

INVENTOR(S): Altmann, Eva; Betschart, Claudia; Gohda, Keigo; Horiuchi, Miyuki; Lattmann, Rene; Missbach, Martin; Sakaki, Junichi; Takai, Michihiro; Teno, Naoki; Cowen, Scott Douglas; Greenspan, Paul David; McQuire, Leslie Wighton; Tommasi, Ruben Alberto; Van Duzer, John Henry

PATENT ASSIGNEE(S): Novartis AG, Switz.; Novartis-Erfindungen Verwaltungsgesellschaft mbH

SOURCE: PCT Int. Appl., 137 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9924460	A2	19990520	WO 1998-EP6937	19981103
WO 9924460	A3	19990902		
W:	AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
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AU 9914873	A1	19990531	AU 1999-14873	19981103
AU 751669	B2	20020822		
EP 1028942	A2	20000823	EP 1998-958887	19981103
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI			
BR 9813197	A	20000829	BR 1998-13197	19981103
TR 200001189	T2	20000921	TR 2000-200001189	19981103
JP 2001522862	T2	20011120	JP 2000-520468	19981103
RU 2201420	C2	20030327	RU 2000-114821	19981103
ZA 9810073	A	19990505	ZA 1998-10073	19981104
TW 527362	B	20030411	TW 1998-87118553	19981105
NO 2000002320	A	20000704	NO 2000-2320	20000502
US 6353017	B1	20020305	US 2000-643639	20000822

US 2004029814	A1	20040212	US 2003-342872	20030115
US 2004110806	A1	20040610	US 2003-694672	20031028
PRIORITY APPLN. INFO.:			GB 1997-23407	A 19971105
			US 1997-108160P	P 19971205
			US 1997-985973	A 19971205
			WO 1998-EP6937	W 19981103
			US 1998-186223	B1 19981104
			US 2000-643639	A1 20000822
			US 2002-54590	B1 20020122
			US 2003-342872	A1 20030115

OTHER SOURCE(S): MARPAT 130:352553

AB N-terminal substituted dipeptide nitriles R(L)xX1NHCR2R3C(:Y)NHCR4R5CN [R is optionally substituted aryl, alkyl, alkenyl, alkynyl, heterocyclyl; R2, R3 = H, optionally substituted alkyl, cycloalkyl, bicycloalkyl, or aryl-, biaryl-, cycloalkyl, bicycloalkylalkyl; R2 and R3 together represent alkylene, optionally interrupted by O, S, or NR6, where R6 is H, alkyl, arylalkyl; or R2 or R3 are linked by alkylene to the adjacent nitrogen to form a ring; R4, R5 = H, optionally substituted alkyl, arylalkyl, CO2R7, CONR7R8 (R7 is optionally substituted alkyl, aryl, arylalkyl, cycloalkyl, bicycloalkyl, or heterocyclyl and R8 is H or optionally substituted alkyl, aryl, arylalkyl, cycloalkyl, bicycloalkyl, heterocyclyl), etc.; R4 and R5 together represent alkylene, optionally interrupted by O, S, or NR6; X1 = CO, CS, SO, SO2, P(O)OR6; Y = O, S; L is optionally substituted Het, Het-CH2, CH2-Het (Het = O, N, or S); x = zero or 1] were prepared as inhibitors of cysteine cathepsins, e.g., cathepsins B, K, L and S, and can be used for the treatment of cysteine cathepsin dependent diseases and conditions. Thus, N-[2-[(3-carboxyphenyl)methoxy]-1(S)-cyanoethyl]-3-methyl-N $\alpha$ -(2,2-diphenylacetyl)-L-phenylalaninamide was prepared and shown to have IC50  $\approx$  5 nM for inhibition of cathepsin B.

IT 225119-70-0P 225120-04-7P 225121-07-3P  
225121-14-2P

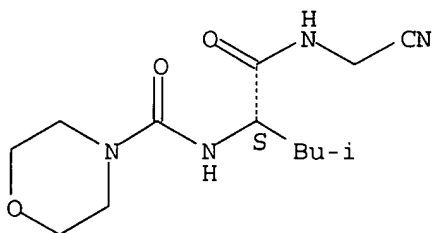
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(synthesis of dipeptide nitriles as inhibitors of cysteine cathepsins)

RN 225119-70-0 CAPLUS

CN 4-Morpholinecarboxamide, N-[(1S)-1-[[[cyanomethyl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

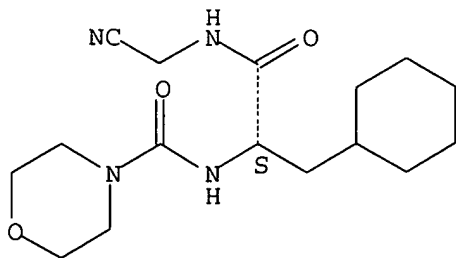
Absolute stereochemistry.



RN 225120-04-7 CAPLUS

CN 4-Morpholinecarboxamide, N-[(1S)-2-[(cyanomethyl)amino]-1-(cyclohexylmethyl)-2-oxoethyl]- (9CI) (CA INDEX NAME)

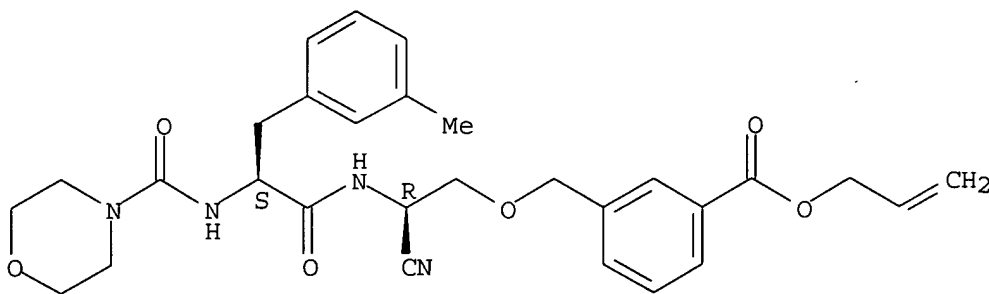
Absolute stereochemistry.



RN 225121-07-3 CAPLUS

CN Benzoic acid, 3-[[[(2R)-2-cyano-2-[[[(2S)-3-(3-methylphenyl)-2-[(4-morpholinylcarbonyl)amino]-1-oxopropyl]amino]ethoxy]methyl]-, 2-propenyl ester (9CI) (CA INDEX NAME)

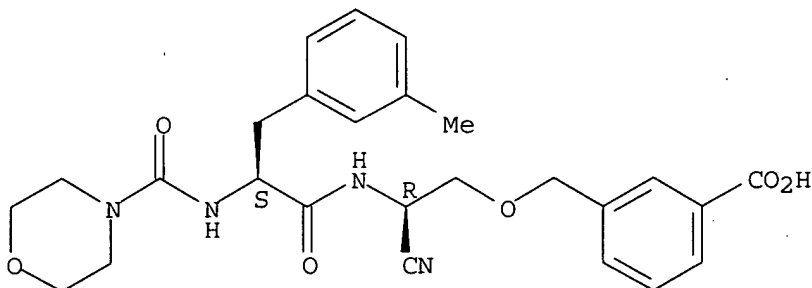
Absolute stereochemistry.



RN 225121-14-2 CAPLUS

CN Benzoic acid, 3-[[[(2R)-2-cyano-2-[[[(2S)-3-(3-methylphenyl)-2-[(4-morpholinylcarbonyl)amino]-1-oxopropyl]amino]ethoxy]methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



=> log y

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

44.91

211.05

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE

TOTAL

ENTRY

SESSION

CA SUBSCRIBER PRICE

-6.57

-6.57

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